آزمایشگاه
دنا
DeNA Laboratory

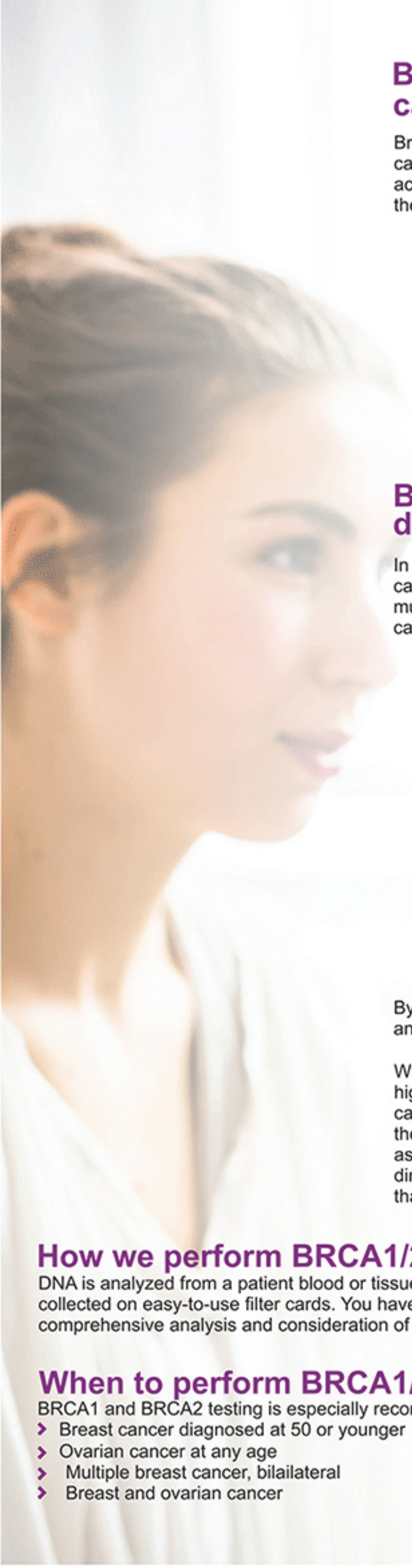
شماره سند:31-1-AG1

BRCA 1/2

Breast cancer testing at CENTOGENE

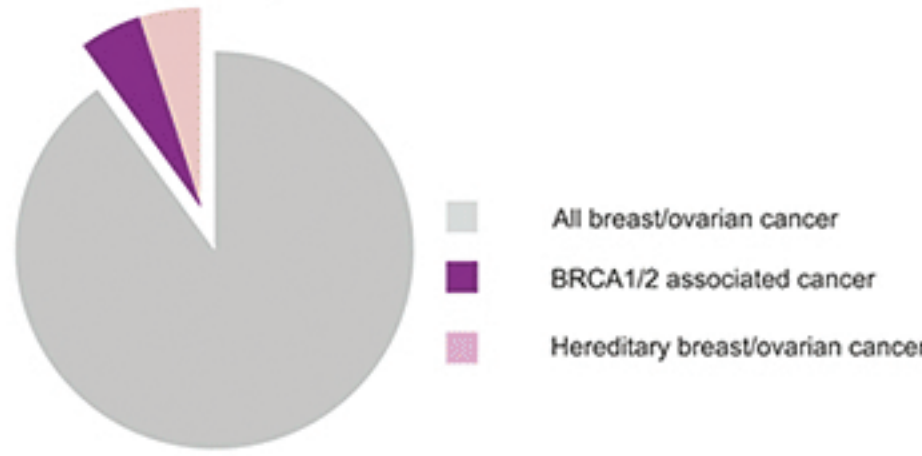
Think about tomorrow, today.

5-10% of patients with breast and/or ovarian cancer have a hereditary form. For any individual carrying a mutation in BRCA1 or BRCA2, the lifetime risk of developing breast/ovarian cancer increases from 12% to 50-85%



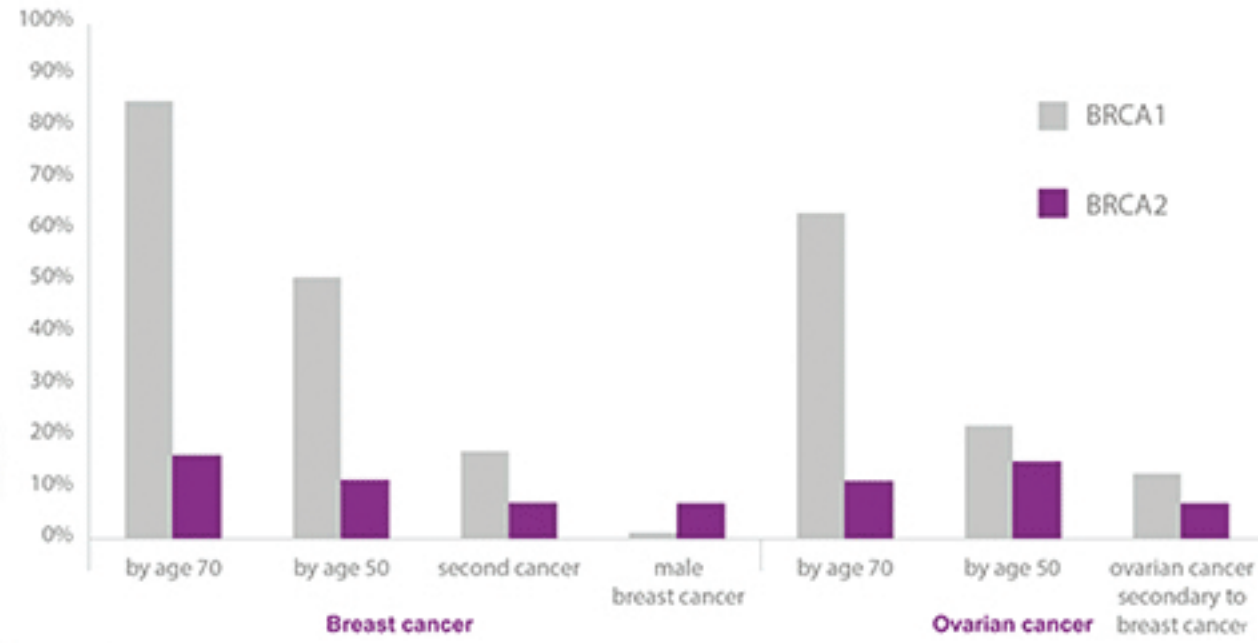
BRCA1/2 are a key factor in breast a ovarian cancer development

Breast and ovarian cancer are common, they are the first and fifth most common cancers that occure in women. Hereditary forms of breast and ovarian cancer account for 5-10% of all cases diagnosed, and an association with mutations in the BRCA1/2 genes has been clearly demonstrated.



BRCA1/2 increase the lifetime risk of developing cancer

In the general population, approximately 12% of women will develop breast cancer in their lifetime. in comparison, 55-65% of women carrying a BRCA1 mutation and 45% of women carrying a BRCA2 mutation will develop breast cancer by age 70.



By detecting cancer early, patient can have timely access to preventative measure and proactive treatment-leading to b better peognosis overall.

Where cancer has been diagnosed, somatic testing of the BRCA1/2 genes is still highly beneficial and can significantly improve the prognosis and quality of life of cancer-affected patients. Somatic mutation analysis of tumors can identify therapeutic sensitizing and resistance mutations. This allows a more detailed assessment of the diagnosis, prognosis and can help identify targeted therapies directed towards the individual patient's tumor profile. For example, new drugs that specifically target the BRCA1/2 signaling pathways have been approved.

How we perform BRCA1/2 testing at CENTOGENE

DNA is analyzed from a patient blood or tissue sample. CENTOGENE can perform genetic testing from dried blood spots collected on easy-to-use filter cards. You have the choice of performing full sequencing of BRCA1 and BRCA2, allowing comprehensive analysis and consideration of every variant detected across both genes.

When to perform BRCA1/2 testing

BRCA1 and BRCA2 testing is especially recommended when a patient's persona; or family history shows any of the following:

- Breast cancer diagnosed at 50 or younger
- Ovarian cancer at any age
- Multiple breast cancer, bilailateral
- Breast and ovarian cancer

- Male breast cancer
- Triple-negative (estrogen receptor negative, progestrone receptor negative and HER2/neu negative) breast cancer
- Pancereatic cancer with breast or ovarian cancer in the same individual, or no the same side of the family
- Two or more relatives with breast cancer, one under age 50
- Three or more relative with breast cancer at any age
- A previously identified BRCA1 or BRCA2 mutation

What are the possible outcomes of the test?

a) Positive:
If the test identifies a disease mutation, then a predisposition to breast and/or ovarian cancer will be confirmed. This does not necessarily mean that the patient has cancer or will develope it. However, depending on the mutation, the patient will have an increased likelihood of developing cancer of between 46-87% over lifetime.

b) Negative:
If the genetic test does not identify a predisposing BRCA1/2 mutation, then the patient's individual risk of developing breast/ovarian cancer is low (the risk of developing breast cancer in the general population is 12%). A negative test result should be discussed to see what individual cancer screening prevention programs might be appropriate for the patient.

c) Inconclusive:
Not all mutations in BRCA1/2 are disease causing. Many disease-causing mutations have been confirmed but not all. In some instances, the test may identify a mutation in BRCA1/2 which cannot be conclusively identified as disease causing.

Test results determine next steps

When a pathogenic BRCA1/2 mutation is detected

Patients with a significantly increased breast cancer risk due to an inherited variant should be informed about possiblities of invidual risk reduction. If a BRCA1/2 mutation is identified, regular screening, prophylactic treatment or surgery are all options that should be discussed with a genetic counselleor and the treating clinician.

Where an inherited mutation in BRCA1/2 is identified in a family, testing of at-risk relatives can identify those family members who also carry the mutation, and may benefit from preventive action. Germline mutations in BRCA1/2 are inherited in an autosomal dominant manner. This means any offspring of an individual with a BRCA1/2 mutation has a 50% chance of inheriting the mutation, and should be offered genetic analysis for the identified variant.

When no clear pathogenic BRCA1/2 mutation is detected

If no mutation in BRCA2 is identified, the following explanations may be considered:

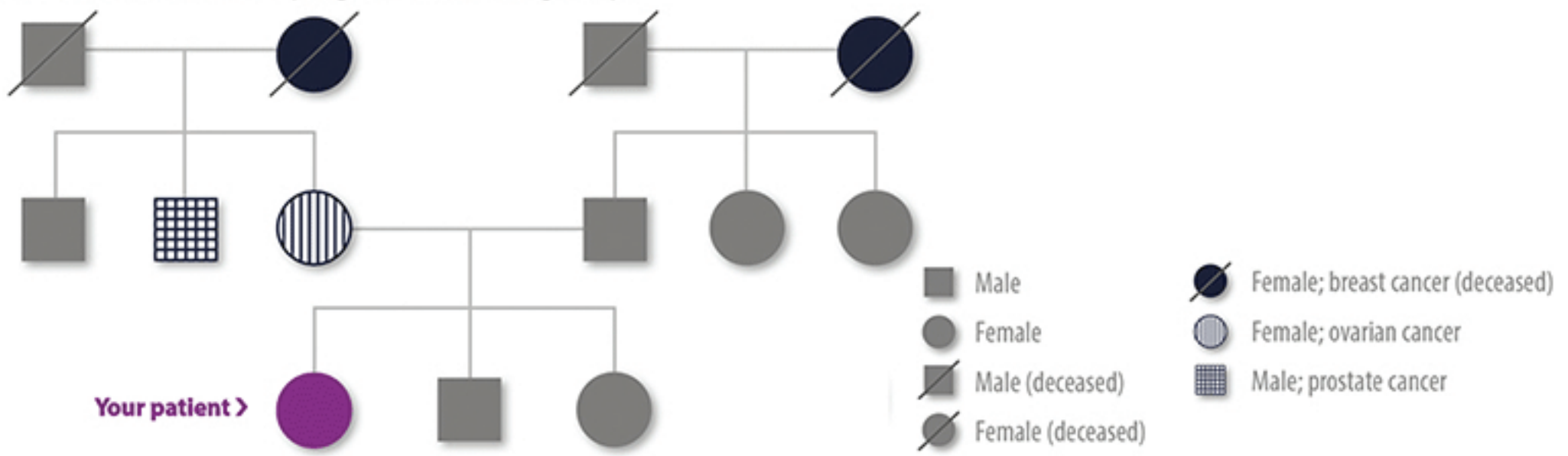
- The case is not due to an inherited BRCA1/2 variant, but is a sporadic case (risk od breast cancer is 12%)
- The causative mutation is in an intron, or in a regulatory element that cannot be identified with routine diagnostic methods.
- Other disorders with elevated risk of breast and/or ovarian carcinoma should be considered (Li-Fraumeni syndrome, Cowden syndrome, hereditary diffuse gastric cancer, Peutz-Jeghers-type hamartomatous polyps)

For patients who are BRCA1/BRCA2 negative, we offer alternative gene panels including additional genes linked to hereditary breast and/or ovarian cancer.

High risk of hereditary breast cancer

Background

Your patient has one 1st degree relative with ovarian cancer (diagnosed before age 50) and one 2nd degree relative with bilateral breast cancer (diagnosed before age 50).



The probability to identify BRCA1/2 mutation is high (approx.30%) due to the family history with mother and aunt diagnosed with breast/ovarian cancer at an early age.

- Identification of a pathogenic variant would confirm the significantly increased lifetime risk for breast and ovarian cancer.
- Genetic counselling needs to be offered
- Individualized surveillance and potential therapy options discussed
- Genetic counselling and carrier analysis to siblings should offered

Accordingly USPSTF BRCA1 and BRCA2 testing is not suggested for healthy women in the absence family history of cancer.

However, as family pedigrees are not always informative, due to smaller families or unavailable information BRCA1/2 screening might also be offered in these case to identify the high risk persons and to offer them the same diagnostic and therapeutic options.

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THE RARE DISEASE COMPANY

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