The impact of hereditary breast and ovarian cancer (HBOC) syndrome testing on patient management and your practice

Use BRACAnalysis® as a guide in your medical and surgical management
BRACAnalysis® testing benefits

FOR YOUR PATIENTS
- Empower patients with knowledge to make informed surveillance, preventive, surgical, and treatment decisions.
- Provide families with useful information on inherited risks.

FOR YOUR PRACTICE
- Comply with International societal guideline recommendations.1-5
- Provide individualized medical management plans for your patients.

INCREASED RISK FOR PRIMARY AND SECONDARY CANCER†

Mutations dramatically increase the risk of developing cancer

AMEANG BREAST CANCER PATIENTS:
76% of women chose to undergo BRCA mutation testing, and 79% of these women used genetic test results to aid in their surgical decision making.6

CHECK PERSONAL OR FAMILY HISTORY† FOR THESE INDICATORS*
- Ovarian cancer
- Breast cancer diagnosed ≤50 years
- Two primary breast cancers§
- Male breast cancer
- Triple negative breast cancer
- Three or more HBOC-associated cancers at any age§,**
- Ashkenazi Jewish ancestry with an HBOC-associated cancer §,**
- A previously identified BRCA mutation in the family

THE UNMET MEDICAL NEED
Only ~10% of BRCA mutation carriers have been identified.7

† For reference and supporting data on risk factors and medical management visit www.myriadgenetics.eu/references

† Close blood relatives include first, second, or third degree in the maternal or paternal lineage.
* Assessment criteria based on medical society guidelines. For these individual society guidelines, go to www.myriadgenetics.eu/professional-practice-guidelines.
§ In the same individual or on the same side of the family.
** HBOC-associated cancers include breast (including DCIS), ovarian and pancreatic, and aggressive prostate cancer (Gleason score of >7).
# The value of test results

## MAKING SENSE OF THE POSSIBLE OUTCOMES OF THE BRACAnalysis® TEST, AND HOW TO PROCEED WITH PATIENT CARE.

### POWER OF A POSITIVE RESULT

**POSITIVE FOR DELETERIOUS MUTATION**

**DIAGNOSIS OF HBOC SYNDROME: INCREASE CANCER RISK**

Follow medical management guidelines for mutation carriers.

- Intensive surveillance initiated in the 20s, including breast MRI
- Preventive drug therapy
- Risk-reducing surgeries

The National Comprehensive Cancer Network and European Society for Medical Oncology (ESMO) are some of the many organizations with published medical management recommendations for BRCA mutation carriers, which include:

### VALUE OF THE NEGATIVE RESULT

**NO DELETERIOUS MUTATION DETECTED**

**NO INCREASED CANCER RISK**

Manage based on general population cancer screening recommendations.

**CHANCE OF HBOC SYNDROME SIGNIFICANTLY REDUCED**

Manage based on negative test result and personal/family history of cancer.

The National Comprehensive Cancer Network and European Society for Medical Oncology (ESMO) are some of the many organizations with published medical management recommendations for these patients.

### POWER OF EXPERIENCE

**GENETIC VARIANT OF UNCERTAIN SIGNIFICANCE (VUS)**

**MANAGE BASED ON PERSONAL/FAMILY HISTORY OF CANCER**

**DEFINING VUS**

A genetic variant of uncertain significance is a variation in the DNA sequence that may or may not contribute to breast or ovarian cancer risk.

**MANAGING THE PATIENT**

Management is to be based on patient’s personal and/or family history of cancer.

**RECLASSIFYING A VARIANT**

When data allows a previously uncertain variant to be reclassified as harmless or deleterious, Myriad Genetics provides an updated report to healthcare professionals.

Myriad has the lowest VUS rate globally with a < 3% VUS rate for BRCA1 / BRCA2 mutations.8
The testing and the surgeries were by far the best decision I ever made. I feel as though I had a chance to look through a crystal ball to see my possible future, and I was able to make choices while I was still healthy.

- Stefanie B.

MEDICAL INTERVENTION GREATLY REDUCES RISK†

Reduce risk of hereditary cancer with proven medical management

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Age to begin</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast self-exam</td>
<td>18 years</td>
<td>monthly</td>
</tr>
<tr>
<td>Clinical breast exam</td>
<td>25 years</td>
<td>twice a year</td>
</tr>
<tr>
<td>Mammography</td>
<td>25 years</td>
<td>yearly</td>
</tr>
<tr>
<td>MRI</td>
<td>25 years</td>
<td>yearly</td>
</tr>
<tr>
<td>TVUS and CA-125*</td>
<td>30 years in patients not electing RRBSO</td>
<td>twice a year</td>
</tr>
</tbody>
</table>

a. NCCN guidelines suggest patients who do not elect RRBSO consider concurrent transvaginal ultrasound (TVUS) and cancer antigen-125 (CA-125) blood testing every 6 months starting at age 30, or 5 to 10 years before the earliest age of first diagnosis of ovarian cancer in the family.

"The testing and the surgeries were by far the best decision I ever made. I feel as though I had a chance to look through a crystal ball to see my possible future, and I was able to make choices while I was still healthy."

- Stefanie B.

It took me 7 years to be tested for the BRCA mutation. It took me fewer than 4 months to have all the prophylactic surgeries to try and prevent becoming a victim of cancer.

- Jodi V.

† For reference and supporting data on risk factors and medical management visit www.myriadgenetics.eu/references

*a. In contralateral breast cancers.
† † For reference and supporting data on risk factors and medical management visit www.myriadgenetics.eu/references
Assess HBOC risk with a proven 4-step protocol

1 SCREEN
   • Screen every patient for personal and family history of cancer/ages of diagnosis
   • Update information annually

2 EVALUATE
   • Assess for indicators
   • Discuss BRACAnalysis® testing with appropriate patient

3 DIAGNOSE
   • Order BRACAnalysis® test using Myriad’s collection kit
   • Interpret result and assign risk

4 MANAGE
   • Establish appropriate medical management plan according to clinical guidelines and recommendations

Myriad Genetics support makes it easy

Our dedicated team of representatives and other staff can provide in-person and online assistance to help you implement BRACAnalysis® testing in your offices.

Medical Support
Myriad offers medical support with a team of highly trained medical specialists, available via phone, email, and in person.

Practice Support
Our representatives help clinical practices in their implementation of genetic testing.

Professional Community Support
Multiple professional guidelines support genetic testing for HBOC syndrome.

<table>
<thead>
<tr>
<th>Professional Society</th>
<th>Website URL</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Comprehensive Cancer Network Genetic/Familial High-Risk Assessment</td>
<td><a href="http://www.nccn.org/professionals/physician_gls/PDF/genetics_screening.pdf">www.nccn.org/professionals/physician_gls/PDF/genetics_screening.pdf</a> (login</td>
</tr>
<tr>
<td>Breast and Ovarian 1</td>
<td>required)</td>
</tr>
<tr>
<td>European Society for Medical Oncology (ESMO)2</td>
<td><a href="http://annonc.oxfordjournals.org/content/22/suppl_6/vi31.full">http://annonc.oxfordjournals.org/content/22/suppl_6/vi31.full</a></td>
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<tr>
<td>BRCA in breast cancer</td>
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<tr>
<td>European Society for Medical Oncology (ESMO)3</td>
<td><a href="http://annonc.oxfordjournals.org/content/22/suppl_6/vi12.full">http://annonc.oxfordjournals.org/content/22/suppl_6/vi12.full</a></td>
</tr>
<tr>
<td>Primary breast cancer</td>
<td></td>
</tr>
<tr>
<td>American Society of Clinical Oncology (ASCO)4,5</td>
<td><a href="http://www.cancer.gov/cancer-types/hereditary-breast-and-ovarian-cancer">http://www.cancer.gov/cancer-types/hereditary-breast-and-ovarian-cancer</a></td>
</tr>
</tbody>
</table>
Professional Community Support

Our representatives help clinical practices in their implementation of genetic testing in person.

Myriad offers medical support with a team of highly trained medical specialists, available via phone, email, and in person. Myriad Genetics support makes it easy to implement BRAC® testing in your offices.

Analysis

Our dedicated team of representatives and other staff can provide in-person and online assistance to help you make the right choices.

BRAC® Analysis® test using Myriad's collection kit

• Interpret result and assign risk

Establish appropriate medical management plan according to clinical guidelines and recommendations.

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Technical information

BRAC® Analysis® is a molecular diagnostic test for hereditary breast/ovarian cancer (HBOC) syndrome and cancers related to mutations in BRCA1 and BRCA2 genes. Genetic testing is performed by both full sequencing and large rearrangement methodologies.

Sequencing: The majority of mutations in the BRCA1 and BRCA2 genes are detected through sequencing technology, which involves sequencing the entire coding region of the gene. BRAC® is located on chromosome 17p13 and is composed of 1863 base pairs in 22 coding exons. Full sequencing is performed in the forward and reverse direction of all coding exons and 500 base pairs of non-coding regions to detect missense, frameshift, nonsense, intron-exon boundaries, deletions, and insertions.

Large rearrangements: Approximately 10% of mutations in high-risk patients (0.5% risk for a deleterious mutation) and 9% of low-risk patients have a large rearrangement in the BRCA1 or BRCA2 gene. Large structural rearrangements (deletions, duplications, etc.) cannot be detected through sequencing technologies. Myriad Genetics utilizes Multiplex Ligation-dependent Probe Amplification (MLPA), a very robust and reliable technology for detecting large rearrangements. These large deletions will be confirmed by additional specific PCR sequencing or CGH analysis.

Test offerings

BRAC® Analysis® sequencing and large rearrangement analysis of the BRCA1 and BRCA2 genes. This test is for people who do not have any known gene mutations in the family.

Single site BRAC® Analysis®: This test is for individuals who already know the BRCA1 or BRCA2 gene mutation in the family. A copy of the result should be given to family members who have not tested positive in order to make informed decisions.

BRAC® Analysis®: This test examines the three most common BRCA1 and BRCA2 gene mutations in individuals of Ashkenazi Jewish (Central/Eastern European) ancestry. These three mutations (617delT in BRCA1 and 5382insC and 6174delT in BRCA2) are present in up to 6.5% of individuals of Ashkenazi Jewish descent. If an individual does not test positive for the three common mutations and has a significant family history, reflex testing to full BRAC® Analysis® should be considered.

References

8. 7. References
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