HEREDITARY BREAST AND OVARIAN CANCER SYNDROME (HBOC) PREVENTION & MANAGEMENT

BRCA1 and *BRCA2* mutations have been shown to increase the risk of several different cancer types such as breast, ovarian, prostate and pancreatic cancers. These mutations can be categorized into two types:

Germline: inherited from either parent and are found in every cell of the offspring.

Somatic mutation: an acquired mutation that is not inherited and found in tumor tissue.

Approximately 55-65% and 39% of patients with deleterious *BRCA1* germline mutations will develop breast or ovarian cancer, respectively, by the age of 70. Approximately 45% and 11-17% of patients with deleterious *BRCA2* germline mutations will develop breast or ovarian cancer, respectively, by the age of 70.[1,2]

GENETIC TESTING

Genetic testing may be performed in high-risk individuals to determine the presence of deleterious germline mutations. Targeted multiple-gene panels are often used for cancer patients and test for many inherited or somatic mutations at one time.[1,2] The NCCN Guidelines recommend that the following individuals be tested for *BRCA1/2* mutations:[3]

Affected individuals with any of the following:

- ☐ Mutation identified in family member
- ☐ Breast cancer diagnosed ≤45 yo
- ☐ Breast cancer diagnosed ≤50 yo with:
  - ☐ An additional breast cancer primary
  - ☐ ≥1 close relative* with breast or pancreatic cancer
  - ☐ ≥1 relative with prostate cancer (Gleason score ≥7)
  - ☐ An unknown or limited family history
- ☐ Triple negative breast cancer diagnosed ≤60 yo
- ☐ Breast cancer diagnosed at any age with:
  - ☐ ≥2 close relatives* with breast cancer, pancreatic cancer, or prostate cancer (Gleason score ≥7) at any age
  - ☐ ≥1 close relative* with breast cancer diagnosed ≤50 yo
  - ☐ ≥1 close relative* with ovarian cancer
  - ☐ Close male relative* with breast cancer
  - ☐ Ashkenazi Jewish ethnicity
- ☐ Male breast cancer
- ☐ Ovarian, fallopian tube or primary peritoneal cancer
- ☐ Prostate cancer (Gleason score ≥7) or pancreatic cancer at any age with ≥1 close relative* with ovarian cancer at any age or breast cancer ≤50 yo or two relatives with breast, pancreatic or prostate cancer (Gleason score ≥7) at any age
- ☐ Pancreatic cancer and Ashkenazi Jewish ancestry
- ☐ *BRCA1/2* mutation detected by tumor profiling in absence of germline mutation analysis

Unaffected individuals (ie, no cancer diagnosis) with any of the following family history should be considered for testing when an appropriate family member is unavailable for testing:

- ☐ Third-degree relative who has breast cancer and/or ovarian cancer and who has ≥2 close relatives* with breast cancer (at least one close relative* diagnosed ≤50 yo) and/or ovarian cancer
- ☐ First- or second-degree relative meeting any of the "affected" criteria

**Close blood relatives include first-, second-, and third- degree relatives on the same side of family;*
All recommendations are category 2A unless otherwise indicated.

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GENETIC COUNSELING[1]

Genetic counseling is generally recommended before and after any genetic test for an inherited cancer syndrome. This counseling should be performed by a health care professional who is experienced in cancer genetics. Genetic counseling usually covers many aspects of the testing process, including:

- ☐ A hereditary cancer risk assessment based on an individual's personal and family medical history
- ☐ Discussion of:
  - ☐ The appropriateness of genetic testing
  - ☐ The medical implications of a positive or a negative test result
  - ☐ The possibility that a test result might not be informative
  - ☐ The psychological risks and benefits of genetic test results
  - ☐ The risk of passing a mutation to children
- ☐ Explanation of the specific test(s) that might be used and the technical accuracy of the test(s)

BRCA MUTATION POSITIVE MANAGEMENT[3]

WOMEN

At detection of *BRCA* mutation: Discuss option of risk-reducing mastectomy (counsel on degree of protection, reconstruction options, and risks).

25 yo	Begin clinical breast exam every 6-12 months
25-29 yo	Begin annual breast MRI screening with contrast or mammogram if MRI unavailable
30-75 yo	Annual breast MRI screening with contrast and mammogram
35-40 yo	Recommend risk-reducing salpingo-oophorectomy (RRSO) upon completion of child bearing (may delay until 40-45 yo in patients with *BRCA2* mutations who have already maximized their breast cancer prevention).*

**For those patients who have not elected RRSO, transvaginal ultrasound and/or serum CA-125 may be considered at the clinician's discretion starting at age 30-35 yo.*

MEN

35 yo	Breast self-exam training and education, as well as clinical breast exams every 12 months
45 yo	Recommend prostate cancer screening for *BRCA2* carriers; Consider prostate cancer screening for *BRCA1* carriers.

MEN AND WOMEN: No specific guidelines exist for pancreatic cancer and melanoma, but may consider full-body skin and eye exam.

A positive genetic test result may also have important health and social implications for family members, including future generations. Unlike most other medical tests, genetic tests can reveal information not only about the person being tested but also about that person's relatives. It is important to consider family planning in addition to preventative and screening measures the *BRCA* mutation positive patient should take. Medical records need to be updated with family history if new cancers are diagnosed in family members. Recommend genetic counseling and consideration of genetic testing for at-risk relatives.[1]

References:
[1]https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet;
[2]https://www.cancer.gov/about-cancer/causes-prevention/genetics;
[3]NCCN Guidelines Version 2.2017: Breast and Ovarian Genetic Assessment.

NEED TO REFER A PATIENT?

Visit www.nsgc.org/page/find-a-gc-search to find a genetic counselor in your area