

## Management Recommendations and Risk Reduction Options for Transgender Females with *BRCA1* and *BRCA2* Mutations

### Terminology

- Cisgender man/male: An individual who was assigned male at birth and identifies as male.
- Cisgender woman/female: An individual who was assigned female at birth and identifies as female.
- Transgender woman/female: An individual who was assigned male at birth but their gender identity is female.

Genetic testing for mutations in *BRCA1* and *BRCA2* has been performed for over twenty years. Transgender women with a *BRCA1* mutation have a slightly increased lifetime risk to develop breast cancer; however, the exact cancer risk is unknown. Transgender women with a *BRCA2* mutation have approximately a 5-10% lifetime risk to develop breast cancer. These estimations are based on the lifetime breast cancer risks from data collected from cisgender men with a *BRCA1* or *BRCA2* mutation, respectively.

Transgender women with a *BRCA1* or *BRCA2* mutation may also be at increased risk to develop prostate cancer, although, the exact risk is unknown. There is some data to suggest BRCA-associated prostate cancers may also be more aggressive. There is also an increased risk for pancreatic cancer and melanoma, with the risk being highest in individuals with *BRCA2* mutations, as compared to those *BRCA1* mutations.

The risks and screening recommendations for BRCA1/2-associated cancers for transgender women depend on the type of hormonal and surgical interventions performed for gender transition.

### Hormone Therapy

Hormonal therapy is typically prescribed for transgender women to induce breast formation. This could be either estrogen-only hormone therapy or estrogen plus progestin hormone therapy. In individuals who have received hormonal therapy, breast development is generally irreversible; although, breast size may decrease if estrogen is discontinued.

### **Hormone Therapy and Breast Cancer Risk**

- At this time, there is limited research regarding the risk of breast cancer in transgender women with BRCA1/2 mutations using hormone therapy, but the risk may be higher than in cisgender men or transgender women with a BRCA1/2 mutation. When applying what we know from the research about the association of breast cancer risk and hormone therapy in cisgender women, we know that the use of combined estrogen and progesterone therapy is associated with a higher risk for breast cancer than the use of estrogen therapy alone.
- Longer duration of hormone exposure (i.e. number of years taking the hormone) and the use of progestin likely influence the level of risk.
- A consultation with an oncologist should be considered prior to hormone use.

### **Breast Cancer Screening and Risk-reduction options**

At this time, there is lack of consensus regarding appropriate breast cancer screening and risk-reduction options in transgender women. The following recommendations may differ for each individual due several factors, such as presence of breast tissue, type and duration of hormone use, and use of breast implants. Therefore, it is important to meet with a provider who specializes in hereditary breast cancer to review and discuss medical management recommendations for individualized care.

### **Medical management options for breast cancer risk reduction in individuals without breast tissue and a BRCA1/2 mutation includes:**

- In those without breast tissue and in the absence of hormone therapy or breast implants, mammogram screening is not indicated for transgender women with a BRCA1/2 mutation.
- However, similar to the breast cancer risk management options for cisgender men with a BRCA1/2 mutation, annual clinical breast exam should be performed and monthly self-breast exam beginning at age 35 should be considered.

### **Medical management options for breast cancer risk reduction in those with a BRCA1/2 mutation who have used hormone therapy:**

- There is a lack of consensus regarding breast cancer screening for transgender women who have used hormone therapy.
- The recommendations may differ for individuals based on the duration and type of hormone therapy used, presence of breast tissue, and use of breast implants.

### **Considerations regarding breast augmentation through implants in those with a BRCA1/2 mutation:**

- In transgender women, additional breast development through breast augmentation using implants, after hormone therapy, has not shown to further increase the risk of breast cancer.
- However, implants may impair the accuracy of a mammogram or clinical breast examination.
- For transgender women with breast implants, it is important for them to discuss with their physicians and/or mammogram technologists, so that the mammography machine can be adjusted to get the best image of the natural breast tissue.
- Evaluation of the implant itself is usually performed once every two to three years with a breast ultrasound or non-contrast MRI.

### **Prostate Cancer Screening**

- Since the prostate is usually not removed with gender affirmation surgery, prostate cancer screening through annual blood test (PSA) and rectal exams (DRE) is recommended for individuals with a *BRCA2* mutation beginning at age 40. Prostate cancer screening can be considered for individuals with a *BRCA1* mutations; also beginning at age 40.

### **Family Planning, Reproductive Options, and Reproductive Risks**

#### **Fanconi Anemia and BRCA2 mutation**

Rarely, a child can inherit two *BRCA2* mutations, one from each parent. This causes a different hereditary syndrome known as Fanconi Anemia. Children with Fanconi Anemia are at increased risk to develop bone marrow failure, leukemia, and other cancers, as well as physical differences such as changes in the thumb, small skull size, and short stature. For this reason, individuals with a *BRCA2* mutation who are of reproductive age may wish to consider having their partners tested for mutations in the *BRCA2* gene before becoming pregnant. If both parents have a *BRCA2* mutation, then there is a 25% risk their children will have Fanconi Anemia. We would be happy to coordinate testing through our office or provide information about genetic clinics in their area.

#### **Sperm preservation**

Decisions about family planning (i.e. whether, how, and when to have children) are personal to everyone, regardless of whether or not they have a genetic condition. Some individuals with a *BRCA1/2* mutation who are interested in having children using their sperm may want to pursue family planning options that can prevent the mutation from being passed to their children.

Individuals planning to have an orchiectomy (removal of the testicles) as a part of transition may want to pursue sperm preservation and discussion of family planning options, such as pre-implantation genetic diagnosis (PGD).

## **References**

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