

Caring for Transgender and Gender Diverse Patients in the Breast Oncology Clinic

This tip sheet is based on a presentation given by Ole-Petter R. Hamnvik, MB BCh BAO, MMSc, Director of Education, Center for Transgender Health Brigham and Women's Hospital Boston, MA, USA

Summary

Health care providers will encounter transgender and gender diverse patients in the breast cancer clinic. It is imperative to treat them with respect and provide optimal treatment for their cancer in the setting of gender-affirming care.

Terminology

It is important to use the correct terms to promote precise communication with patients.

Gender identity:	A person's inner sense of being a man, woman, something else, or no gender.
Sex assigned at birth:	The sex recorded at birth, generally based on appearance of external genitalia. These include assigned female at birth (AFAB) and assigned male at birth (AMAB).
Transgender and gender diverse (TGD):	People whose gender identify differs from what is typically associated with their sex designated at birth.
Gender incongruence:	ICD-11 (WHO) term that replaces several outdated terms including transsexualism, gender identity disorder, gender dysphoria.
Trans woman:	AMAB person whose gender identity is female.
Trans man:	AFAB person whose gender identity is male.
Nonbinary:	Gender identity falling outside the traditional binary of man/woman. People who self-identify as nonbinary may identify and present themselves as both or alternatively male and female, as no gender, or as a gender outside the male/female binary.

Gender-Affirming Hormone Therapy (GAHT)

The primary goal of GAHT is to help the patient affirm their gender identity by promoting a physical appearance that is more congruent with their gender identity.

GAHT for Trans Women AMAB

For trans women AMAB, estradiol forms the foundation of GAHT. Formulations are shown below. The doses shown are typical starting doses, which are subsequently titrated to effect and serum hormone levels for each patient.

Tablet 1-2 mg BID	Patch 100 mcg BIW	IM/SC injection 4 mg weekly	Gel/spray
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It is important to titrate to achieve the target estradiol level of 150-300 pg/mL (though there is some controversy and there are some limitations to this).

Estradiol alone is usually not sufficient, as it will often only suppress endogenous testosterone levels to target levels (<50) if estradiol levels are higher than the target. Thus, estradiol is usually given in combination with spironolactone, a steroid hormone receptor blocker. In rare cases, estradiol may be given in combination with leuprolide, a GnRH agonist.

Side effects of estrogen-based hormone therapy are rare, and include:

- Estradiol: venous thromboembolism; possibly increased risk of breast cancer
- Spironolactone: creatinine elevation; elevated potassium
- Leuprolide: low libido; decreased motivation

Initiation of estrogen-based therapy begins to produce physical changes within several months. These include decreased libido (1-3 months), body fat redistribution (3-6 months), decreased muscle mass (3-6 months), and breast growth (3-6 months). However, for many of these changes, maximum effect is only achieved after several years of continuous therapy.¹

GAHT for Trans Men AFAB

For trans men AFAB, testosterone forms the foundation of GAHT. Formulations are shown below. The doses shown are typical starting doses, which are subsequently titrated to effect and serum hormone levels for each patient.

Gel: 40.5 mg of 1.62% qAM	IM/SC injections: 40 mg SC weekly
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It is important to titrate the dose to achieve levels in the male reference range (400-700 ng/dL). Lower target testosterone levels are acceptable if less-than-complete masculinization is desired.

Much like with estrogen-based therapy, the physical effects of testosterone-based therapy begin to appear within several months. These include cessation of menses (1-6 months), vaginal atrophy (1-6 months), increased muscle mass (6-12 months), and growth of facial and body hair (6-12 months). The maximum effect is achieved after several years of sustained therapy.¹

Side effects of testosterone-based hormone therapy are rare, and include:

- Polycythemia, acne
- Aromatization to estrogen – possible concern for estrogen-responsive diseases

Transgender Surgery

In addition to GAHT, embodiment goals may require transgender surgeries.

Masculinizing surgeries include:

Mastectomy	Hysterectomy/oophorectomy	Reconstructive procedures: metoidioplasty, phalloplasty
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Feminizing surgeries include:

Facial feminizing surgery	Breast augmentation	Orchiectomy	Reconstructive procedures: vaginoplasty, vulvoplasty
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Other surgical procedures may be included as indicated.

Breast Cancer Screening Recommendations for Trans Men

Endocrine Society¹

- Conduct subareolar and periareolar annual breast examinations if mastectomy performed
- If mastectomy is not performed, then consider mammograms as recommended by the American Cancer Society²

UCSF Gender Affirming Health Program³

- Transgender men who have not undergone bilateral mastectomy, or who have only undergone breast reduction, should undergo screening according to current guidelines for non-transgender women
- The risk of breast cancer in residual breast tissues after mastectomy is unknown
- Diagnostic physical exams may be appropriate in the case of new complaints

American Cancer Society recommendations for transgender man with reduction mammoplasty or no chest surgery, ≥40 years of age, average risk (less than 15% lifetime risk of breast cancer)²

- Usually appropriate: digital breast tomosynthesis screening; mammography screening
- Usually not appropriate: breast ultrasound; MRI breast (with or without IV contrast)

American Cancer Society recommendations for transgender man with bilateral mastectomies (“top surgery”) at any age and at any risk²

- Usually not appropriate: digital breast tomosynthesis screening; mammography screening; breast ultrasound; MRI breast (with or without IV contrast)

American College of Obstetricians and Gynecologists recommendations for trans men⁴

- Earlier screening
 - Age 30 in those at intermediate (15-20%) lifetime risk of breast cancer, including those with personal history of breast cancer, lobular neoplasia, or atypical ductal hyperplasia
 - Age 25 in those at high ($\geq 20\%$) lifetime risk of breast cancer, including those with genetic predisposition, chest irradiation age 10-30
- Review operative reports to ensure that mastectomy was performed and not just breast reduction
- Offer genetic counseling before surgery for those with a personal or family history of breast cancer or ovarian cancer.

Breast Cancer Screening Recommendations for Trans Women

Endocrine Society¹

- Transgender women with no known increased risk of breast cancer follow breast screening guidelines recommended for non-transgender women

UCSF Gender Affirming Health Program³

- Screening mammography every 2 years once the following criteria have been met
 - Age ≥ 50
 - Minimum of 5 years of feminizing hormone use (10 years appropriate in some patients)

American Cancer Society recommendations for average risk transgender women: ≥ 40 years of age with past or current hormone use equal to or greater than 5 years.²

- May be appropriate: digital breast tomosynthesis screening; mammography screening
- Usually not appropriate: breast ultrasound; MRI breast (with or without IV contrast)

American Cancer Society recommendations for high-risk transgender women: 25-30 years of age or older with past or current hormone use equal to or greater than 5 years. Personal history of breast cancer or chest irradiation at 10-30 years of age, genetic predisposition to breast cancer, family history of breast or ovarian cancer, untested patient with first-degree relative with genetic predisposition to breast cancer.²

- Usually appropriate: digital breast tomosynthesis screening; mammography screening
- Usually not appropriate: breast ultrasound; MRI breast (with or without IV contrast)

Are there direct effects of testosterone on tumor growth?^{5,6,7}

- Higher **androgens** in postmenopausal women are associated with higher breast cancer risk
- >70% of breast cancers are androgen receptor-positive (AR+)
- However, AR expression is associated with better breast cancer outcomes
- Preclinical models of AR activation
 - ER+/AR+ cell line: inhibit growth
 - ER-/AR+ cell line: promote growth
- In several small phase 1/2 trials, AR antagonists have shown no or minimal benefit in breast cancer patients
- Could estradiol from **testosterone** aromatization be problematic?
 - Overall estradiol exposure is lower than in premenopausal women, but higher than postmenopausal women
 - In cases where endocrine therapy would be useful in cisgender women, consider their use in transgender women
 - Testosterone should suppress ovarian function, but the effects are variable. Can combine with leuprolide or oophorectomy.
 - Tamoxifen is preferred hormonal therapy in patients taking testosterone, but aromatase inhibitors can be considered in select cases after thoughtful consideration
- Does cancer increase the risk of testosterone side effects?

Creating a Welcoming Environment

Creation of a welcoming environment is key to patients' wellbeing. It is important to recognize and, if necessary, modify:

Your own behaviors

- Know the basics of language, treatments
- Ask for pronouns, names, other important pieces of information without assumptions, only what is truly needed
- Apologize if you make errors, and then quickly move on
- Understand the impact of prior negative experiences; "routine" might be uncomfortable

The environment

- Training for you, front desk staff, everyone else
- Displays including flags, pictures, brochures, rainbow stickers, pronoun pins
- Gender-neutral bathrooms
- On forms, ensure options that apply to each patient: sex assigned at birth, gender identity, pronouns, name

Electronic Medical Record (EMR)

- Enter information into EMR and make sure that it flows into sticker printers, main page, etc.
- Be careful with all text or dotphrases that include name or pronouns
 - Honorifics: .SALUTATION / .M: Avoid, simply use name, consider “Mx.”
 - Name: use “preferred” name, not legal name. Avoid .NAME, use .PREFNAME.
 - Pronouns:
 - Can use .SHEHERHERS (or.HEHIMHIS or .THEYTHEMTHEIRS) to pull in chosen pronouns
 - For templates, use .HE, .HIM, .HIS (or .SHE, .HER. or .THEY, .THEM.THEIR)
 - For your note, consider searching for wrong pronouns and correct before saving.

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