

SERMs for gender-affirming care

Selective Estrogen Receptor Modulators (SERMs) can activate or inhibit the action of estrogen receptors in various target tissues. [9] Tamoxifen, a first-generation SERM and one of the first available medications of the class is well known for its use in breast cancer [9] and may also be utilised in the treatment of gynecomastia in those assigned male at birth (AMAB). [3] The inhibitory effect of SERMs on estrogen receptors in breast tissue and the activating effect in other tissues make them an interesting option for gender diverse AMAB individuals who seek partial feminization without breast tissue development. As such they have been previously proposed as a treatment option for non-binary individuals. [12]

What are the proposed benefits?

Though not studied for feminization in AMAB individuals, several studies in the AFAB population indicate possible benefits for partial feminization in some tissues:

Raloxifene seems to increase skin elasticity [10] and body fat redistribution [2] in post-menopausal AFAB individuals, which may meet the goals of care of certain transfeminine or non-binary individuals.

As SERMs may potentially increase testosterone levels due to their action on the hypothalamic-pituitary-testicular axis [8], initiation with an androgen blocker such as cyproterone or spironolactone would be advised. In this case SERMs would also play a role in mitigating loss of bone mineral density; Two SERMs, Raloxifene and Lasofoxifene, have shown benefits in the treatment of osteoporosis. [5] However, comparison of Raloxifene to low-dose HRT in postmenopausal osteoporosis suggest that SERMs are not quite as effective as estrogen for bone turnover. In the case of one non-binary AMAB teenager, an ethics panel found the use of SERMs to be the “most ethically justifiable option” to promote bone health while suppressing puberty long term with GnRHa treatment, though there are no studies on the use of SERMs with puberty blockers. [7] SERMs may also have a positive effect on lipid profiles. [9]

While not approved for the above uses in AMAB individuals, patients and some clinics report the use of SERMs for gender affirming care and have found “good effect” in limiting breast growth [6], while others report slowed but still present growth.

What are the side effects?

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In general, SERMs are known to cause hot flashes and increase the risk of uterine cancer (though not relevant for this population) [9], as well as some reports of ophthalmic disease, particularly cataracts with Tamoxifen.

Both Tamoxifen and Raloxifene have been shown to increase VTE risk [4], though most studies have been conducted in older post-menopausal AFAB individuals and those being treated for breast cancer.

Raloxifene seems to have a somewhat smaller risk of VTE. [11] Some studies have also shown Tamoxifen to have a negative impact on cognition in women being treated for breast cancer, though other studies have not. [1]

Conclusion

While the effects of SERMs in AMAB individuals are not fully known, studies in the AFAB population suggest utility for partial feminization in certain tissues, making them an interesting option for gender affirming care in transfeminine and non-binary individuals who do not desire breast growth, the alternative being surgical removal of breast tissue with feminizing HRT.

Raloxifene seems to have the most evidence for skin and body changes with some benefit to bone density as well as a better safety profile. Anecdotally it seems to be more desired by patients. When combined with an androgen blocker it could be a potential treatment option for patients whose goals of care align with the above. A potential regime would be to introduce a typical androgen blocker with Raloxifene 60 mg po daily, some patients in online forums also report trial of this with or without low dose estradiol for further feminization while still attempting to limit breast development.

References

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