

Menopausal hormone therapy and estrogen sensitive cancers

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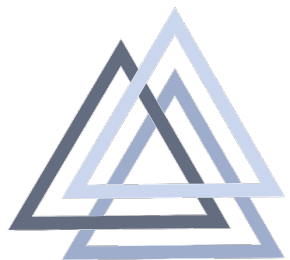


Disclosure

Kesavan: no disclosures

Pinkerton

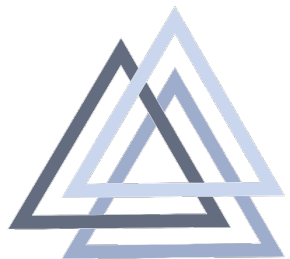
- Multicenter Clinical Trial with Bayer
- Non hormone Hot flash trial
- Neurokinin Receptor Antagonist
- Fees to UVA



Learning Objectives

Develop and utilize an algorithm about effective treatment options, hormonal and nonhormonal, for those with breast cancer risk mutations who are considering early surgical menopause

Identify symptoms of menopause and understand effective and current treatments

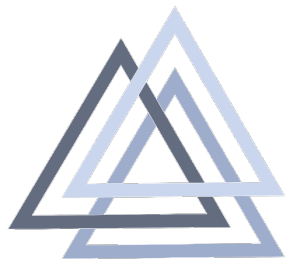


Background

With the advent of increasingly personalized cancer diagnosis and treatment genetic testing is becoming more common .

BRCA1 and BRCA2 mutation carriers have significantly increased risks of developing breast or ovarian cancer in their lifetime.

Risk reducing BSO is often recommended between age 35-40 or when childbearing is complete.

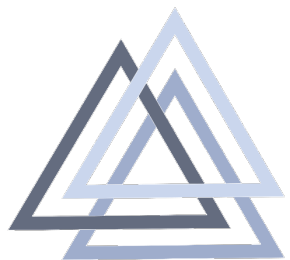


Background

Prior studies have demonstrated that post-menopausal women may experience low quality of life secondary to vasomotor

Hormone replacement therapy can alleviate these symptoms

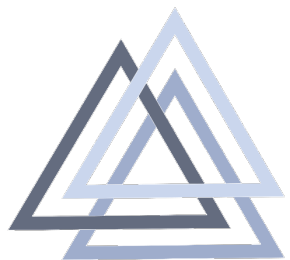
Dedicated counseling and more knowledge targeting their risks of early surgical menopause and risks and benefits of hormone therapy



Background

Education is needed about health risks and types of menopausal symptoms that occur with early menopause

What is needed is a guided process for effective treatment options whether hormonal or nonhormonal.



Pathophysiology

- ER and PR receptors are located throughout the body
- Detrimental effects especially premenopausal with evidence of early demise, increased risk of cardiovascular disease, dementia, decreased quality of life with vaginal dryness



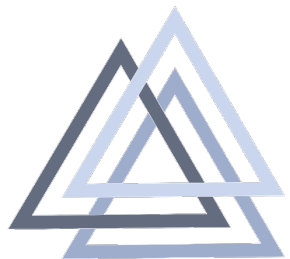
Methods

Phase 1:

Review literature on use of hormone therapy after early surgical menopause for breast cancer gene mutations such as BRCA genes.

Phase 2

Develop an algorithm and test it in high risk clinic and survey benefits on improving education about early menopause and options for therapy and decreasing fear of the surgery.

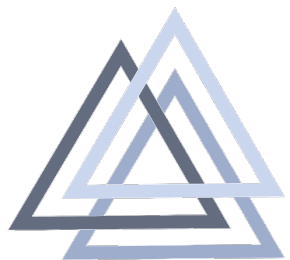


Methods

Phase 1:

Review literature on use of hormone therapy after early surgical menopause for breast cancer gene mutations such as BRCA genes.

Evaluated > 50 papers via PubMed as well as previously established algorithms



Recommendations

Table 1: Premenopausal patient with risk reducing surgery.

—	With Uterus	Without uterus	Symptoms management							
Hormone Replacement therapy			Vaginal dryness	Mood changes	Hot flashes	Weight gain	Recurrent UTI	Bone density loss	Cardiovascular disease	Cognitive effects
First Line	Transdermal estrogen +progestin IUD or oral micronized progesterone Or Conjugated estrogen with the SERM bazedoxifene	Transdermal estrogen preferred over oral for more stable hormone levels	Vaginal moisturizer /lubrication	Venlafaxine escitalopram	Venlafaxine escitalopram , Paroxetine salt 7.5 mg Gabapentin to 900 mg	Diet/exercise changes Nutritional counseling	Vaginal estrogen	Vit D supplementation 1200 mg calcium between diet and supplement, and weight bearing exercise or strength training DEXA baseline	Check lipids, glucose, blood pressure; assess family history	7 hours sleep Exercise Mediterranean diet, Stress reduction
Second line	OCPs		Vaginal hormone-estrogen or intravaginal DHEA	Other SNRI/SSRI	Neurokinin 3 inhibitor for moderate to severe	Transdermal estrogen >oral	Methenamine Post coital antibiotic prophylaxis	Bisphosphonates or denosumab		
Less preferred	Oral estrogen + progestin IUD/oral progesterone		Ospemifene		Paroxetine – other doses, nerve block	Newer weight loss medications		SERM such as Tamoxifen or Raloxifen		
All patients should be offered HRT in this setting to improve overall health and wellbeing. If contraindicated can consider symptoms management. No evidence of HRT specifically for cardiovascular or cognitive effects										



Recommendations

Table 2: Post menopausal patients with remote history of high-risk condition.

	Hormone replacement therapy	Symptoms management							
		Vaginal dryness	Mood changes	Hot flashes	Weight gain	Recurrent UTI	Bone density loss	Cardiovascular disease	Cognitive effects
First Line	Systemic hormone therapy not recommended except in special circumstances	Vaginal moisturizer /lubrication	Venlafaxine	Venlafaxine	Diet/exercise changes	Vaginal estrogen	Vit D supplementation and weight bearing exercise	Nothing additional recommended	Nothing additional recommended
Second line		Vaginal estrogen	Other SNRI	Neurokinin 3 inhibitor	Transdermal estrogen	Methenamine	Bisphosphonate		
Less preferred				Paroxetine, nerve block	Oral estrogen	Post coital antibiotic prophylaxis	SERM		



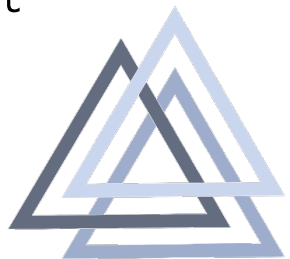
Treatment Options

Estrogen supplementation

- Transdermal estrogen preferred. Start with low dose

Progesterone supplementation

- Protective of uterus- progestin IUD, micronized progesterone or least preferred synthetic progestins
- Niche product conjugated estrogen with bazedoxifene- no increased breast tenderness or density



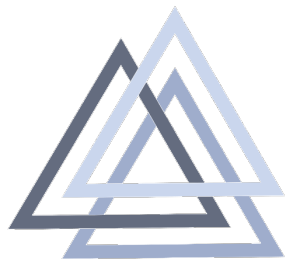
Treatment Options

Oral contraceptive pills

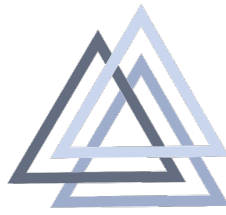
- Not preferred for hormone supplementation as slight increased risk of breast cancer
- Genitourinary Syndrome of Menopause

Vaginal estrogen

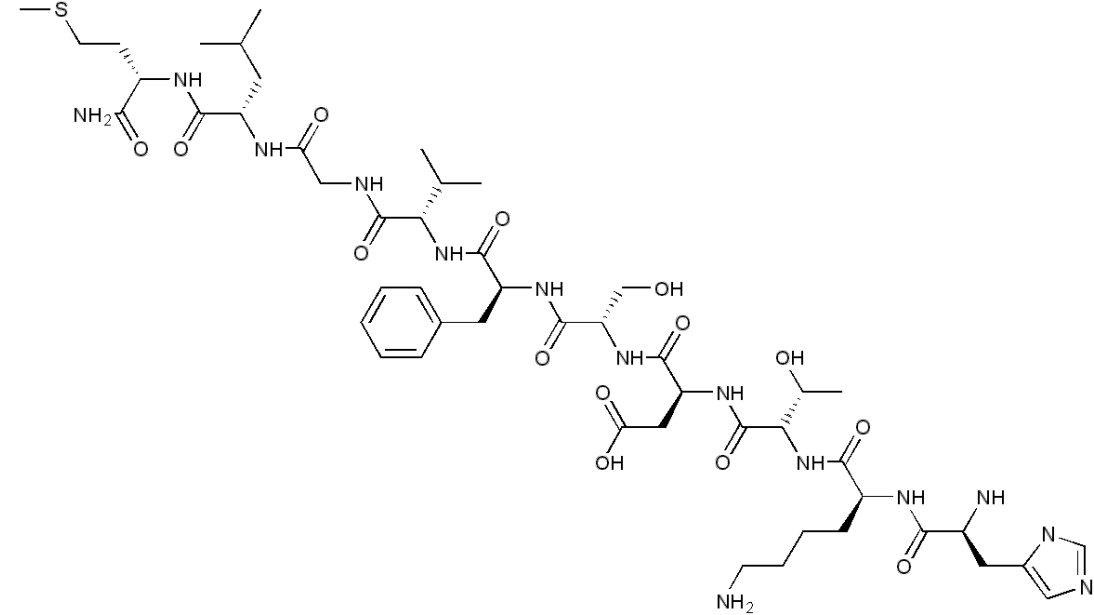
- Primary lubricants and moisturizers
- Low overall systemic absorption.
- Do not recommend vaginal hormone therapy in setting of aromatase use



Treatment Options



- **SNRI**
 - Decreases hot flashes. SSRIs with more off target effects
- **Neurokinin 3 inhibitor**
 - Decreases hot flashes, however cost prohibitive

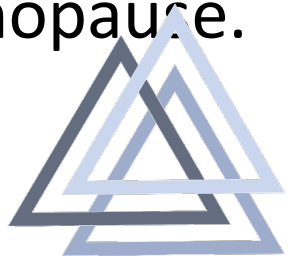


Conclusion

This is an easy-to-use algorithm to help providers and those at high risk navigate these difficult and fear producing decisions.

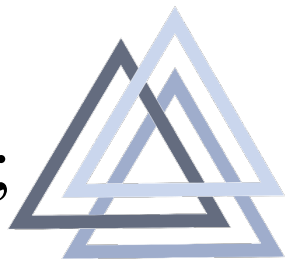
There are many hormonal and non-hormonal options.

These can improve post operative quality of life, improve cardiovascular health and decrease mental anguish secondary to surgery particularly in patients less than 60 years of age and even more so for those with early surgical menopause.



Resources

- 1. Davis SR, Pinkerton J, Santoro N, Simoncini T. Menopause-Biology, consequences, supportive care, and therapeutic options. *Cell*. 2023;186(19):4038-4058. doi:10.1016/j.cell.2023.08.016
- 2. Stuursma A, van Driel CMG, Wessels NJ, de Bock GH, Mourits MJE. Severity and duration of menopausal symptoms after risk-reducing salpingo-oophorectomy. *Maturitas*. 2018 May;111:69-76. doi: 10.1016/j.maturitas.2018.01.012. Epub 2018 Jan 13. PMID: 29673834.
- 3. Faubion SS, Kuhle CL, Shuster LT, Rocca WA. Long-term health consequences of premature or early menopause and considerations for management. *Climacteric*. 2015;18(4):483-91. doi: 10.3109/13697137.2015.1020484. Epub 2015 Apr 7. PMID: 25845383; PMCID: PMC4581591



Thank you! Questions?