HRT after ovarian cancer

Key points

- Use of oral contraceptives is associated with a significant reduction in ovarian cancer risk. (Level I)
- Current and recent use of hormone therapy is associated with a small but statistically significant risk of ovarian cancer in observational studies, principally for serous type, although there was no increase in ovarian cancer risk in women randomized to EPT in the WHI. (Level II)
- In women with a history of ovarian cancer, benefits of hormone therapy use generally outweighs risks, especially with bothersome VMS or early menopause; use of hormone therapy is not advised in women with hormone-dependent ovarian cancers, including granulosa-cell tumors and low-grade serous carcinoma. (Level II)
- Short-term hormone therapy use appears safe in women with *BRCA1* and *BRCA2* genetic variants who undergo risk-reducing BSO before the average age of menopause. (Level II)

Menopause: The Journal of The North American Menopause Society
Vol. 29, No. 7, pp. 767-794
DOI: 10.1097/GME.0000000000002028

NAMS Position Statement

The 2022 hormone therapy position statement of The North American Menopause Society

European Journal of Obstetrics & Gynecology and Reproductive Biology 256 (2021) 492–501

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Editorial

Borderline ovarian tumors: Guidelines from the French national college of obstetricians and gynecologists (CNGOF)

European Journal of Cancer 116 (2019) 35–44

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Current Perspective

Fertility preservation, contraception and menopause hormone therapy in women treated for rare ovarian tumours: guidelines from the French national network dedicated to rare gynaecological cancers

BOT : **HRT can be prescribed after a mucinous or serous BOT**, **caution is recommended after high-risk serous BOT** (invasive peritoneal implants, micropapillary patterns, stromal microinvasion or mucinous tumour with intraepithelial carcinoma)

HRT after BOT

After management of a mucinous BOT, for women under 45 years of age, given the benefit of HRT on cardiovascular and bone risks, and the absence of hormone sensitivity of mucinous BOTs, it is recommended to propose HRT (grade C). After management of a mucinous BOT, for women over 45 years of age, there is no reason to contraindicate the use of HRT. In case of a climacteric syndrome, and as part of an individual assessment of the benefit to risk balance, HRT may be prescribed (Grade C). After management of a serous BOT, with pejorative histological criteria (implants): given the increased risk of recurrence in an invasive hormone-sensitive form, no recommendation on the use of an HRT can be made. The prescription of HRT must be considered with caution, according to an individual risk to benefit balance, as part of a shared medical decision and after discussion in a multidisciplinary meeting including surgeons, pathologists and gynecologists. The elements that could guide the prescription could be the type of implant (invasive or not), the association with other pejorative histological criteria (micropapillary, micro-invasion), the precocity of the menopause. In case of an unfavourable benefit –risk balance for HRT, vaginal local estrogens and/or non-hormonal management of the climacteric syndrome should be proposed, using selective serotonine recapture inhibitors, gabapentine, prégabaline or clonidine. After management of a serous BOT, and in the absence of pejorative histological criteria, there is no reason to contraindicate the use of HRT. In women under 45 years of age without a climacteric syndrome, or in women over 45 years of age with a climacteric syndrome, HRT may be prescribed with regular reassessment of the risk to benefit balance (grade C).

HRT after non gynaecological cancers

Table 2 Categories of cancer types according to oncologic risk (recurrence, progression) of hormone replacement therapy

HRT:	Adavantageous	Neutral (no known negative effect)	Negative effect in certain setting (relative contraindication)	Disadvantageous (contraindicated)
Non-gynecologic cancers	Haematologic malignancies (leukaemias, lymphomas)	(adenocarcinoma??) • Microprolactinoma • Macroprolactinoma (?? – close follow-up required if on HRT)	Brain tumours	• Meningioma • Glioma
	Malignant melanoma (local, cutaneous)		Malignant melanoma (advanced, metastatic)	
	Colorectal cancer		Lung cancer	
	Liver (hepatocellular) cancer	Kidney cancer	Gastric cancer	Gastric cancer (ER+, PR+)
		Thyroid cancer	Bladder cancer	Bladder cancer (ER+)
		Pancreatic cancer		

Hormone Replacement Therapy in Cancer Survivors – Review of the Literature *Pathology & Oncology Research 2020 Deli T et al.*

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2023
Survivorship: Hormone-Related Symptoms

NCCN Guidelines Index
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Discussion

PRINCIPLES OF MENOPAUSAL HORMONE THERAPY (MHT) USE IN FEMALE SURVIVORS[a]

- MHT is the most effective therapy for management of vasomotor symptoms.
- General recommendations are to use the lowest dose possible to control symptoms.
  - Combination estrogen and progestins (for survivors with an intact uterus) or estrogen alone (for survivors without a uterus)
    - ◊ Formulations of hormones include oral, transdermal, vaginal ring, and intrauterine device.
- If MHT is used, refer to appropriate specialist for MHT dosing and management.
- For young cancer survivors experiencing menopause at an early age, consider oral contraceptives or MHT for symptom relief and potential cardiac and bone benefits as long as not contraindicated.
- Relative contraindications for MHT in cancer survivors mirror those for the general population and include:
  - History of hormonally mediated cancers (high-risk endometrial and most breast)
  - History of abnormal vaginal bleeding
  - Active or recent history of thromboembolic event
  - Pregnancy
  - Active liver disease
- Caution in:
  - Survivors with coronary heart disease or hypertension
  - Survivors at increased genetic risk for cancers
  - Survivors who smoke, especially if >35 years

- Approach to treatment should be individualized based on risks and benefits.

Conclusions

Focusing on menopausal symptom and quality of life is an essential part of cancer treatment

-Breast cancer : systemic HRT is generally not adviced. However low-doses vaginal estrogens can be considered (caution in AIs patients)

-Endometrial cancer: HRT seems associated with no increased risk, with the exception of Black American women

-Ovarian cancer: HRT can and should be considered if troublesome menopausal symptoms

-HRT is contraindicated in ESS, leiomiosarcoma and ovarian granulosa tumour

-Women with previous heamatological malignancies, CRC, liver/thiroid/pancreatic/kydney cancer are not controindicated to use HRT

-HRT is contraindicated after brain tumors (in particular glioma and meningioma), gastric/lung/bladder cancer and advanced melanoma

Many non hormonal alternatives are now available for those patients who cannot or do not want to take hormones

Ambulatorio di menopausa e menopausa dopo cancro

SCDU di Ginecologia e Ostetricia
AO MAURIZIANO DI TORINO
Padiglione 5° (piano terra)

Ambulatorio stanza 10 (numero per i medici) 0115082634 (mercoledì mattina)

Segreteria (numero per le pazienti e prenotazioni visite) 0115082384

Grazie per
l'attenzione

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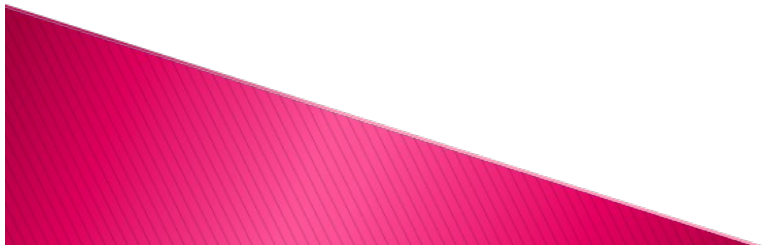


ALTERNATIVE TREATMENS FOR VASOMOTOR SYMPTOMS

- **Antidepressant (SSRIs**: *fluoxetine, citalopram, paroxetine, sertraline and mirtazapine*; **SNRIs**: *venlafaxine and desvenlafaxine)*
- **Anticonvulsants (gabapentin)**
- **Anthypertensives (clonidine)**
- ***New pharmacological perspectives: oxybutynin; elinzanetatnt***
- **Cytoplasmic pollen extract**
- **Black Cohosh**
- **Vitamin E**
- **Phytoestrogen**

- **Acupuncture, yoga, paced respiration hypnosis, diet**

NON-HORMONAL PHARMACOLOGIC TREATMENTS AND DOSING FOR VASOMOTOR SYMPTOMS[a]

Class	Drug	Commonly Used Daily Dose for Management of Vasomotor Symptoms	Comments (For maximum benefit, may increase to higher doses after a week as tolerated)
Antidepressants[b]	Venlafaxine[c] (SNRI) (preferred)	75 mg	Start at lowest dose possible (25 mg or 37.5 mg) and increase as tolerated
	Desvenlafaxine (SNRI)	100 mg	Start at lowest dose possible (25 mg or 50 mg) and increase as tolerated
	Escitalopram (SSRI)	20 mg	• Start at lowest dose possible (10 mg) and increase as tolerated
	Citalopram (SSRI)	20 mg	• Start at lowest dose possible (10 mg) and increase as tolerated
	Sertraline (SSRI)[d]	50 mg	• Start at lowest dose possible (25 mg) and increase as tolerated • Limited data on effectiveness • Use with caution for survivors on tamoxifen
	Paroxetine (SSRI)[d]	Low-dose 7.5 mg or Standard paroxetine short acting up to 20 mg, controlled release up to 25 mg	• Low-dose (7.5 mg) paroxetine is the only FDA-approved alternative to hormones for hot flashes • Use with caution for survivors on tamoxifen
	Fluoxetine (SSRI)[d]	20 mg	• Start at lowest dose possible (10 mg) and increase as tolerated • Limited data on effectiveness • Use with caution for survivors on tamoxifen
Anti-convulsants	Gabapentin[c] (preferred)	900 mg (typically 300 mg 3 times a day)	• Start at lowest dose possible (100 mg or 300 mg) and increase as tolerated • Consider starting at night time as this drug tends to cause sedation
	Pregabalin	150–300 mg	Start at lowest dose possible (25 mg) and increase as tolerated
Alpha-agonist hypertensive	Clonidine	0.1 mg (oral or transdermal)	Transdermal preparations may have fewer side effects
Antimuscarinic anticholinergic	Oxybutynin[1]	5–10 mg	Start with 2.5–5 mg BID, typically used for overactive bladder (OAB) and may cause urinary retention along with other anticholinergic side effects

HRT and Breast cancer: are all the treatements alike?

***Androgenic progestins**, widely used in northern European countries, **have the most negative effect on breast cancer risk** as demonstrated in these studies conducted in Sweden and Denmark*

Magnusson et al. (Int J Cancer.1999)

2563 cases and 2845 controls

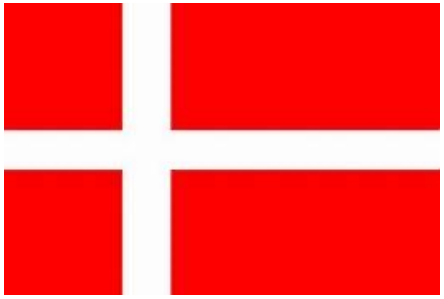
Estrogens	RR = 1.94 (1.47-255)
Estro-progestin	RR = 1.63 (1.37-1.94)

- ☞ **Testosterone-like RR = 1.68 (1.39-2.03)**
- ☞ Progesterone-like RR = 1.14 (0.69-1.88)

Different **Progestins**

Danish Cohort – Stahlbergh et al. (Int J Cancer 2004)

10874 non hysterectomised women; mean use: 7.2±6.3 y 244 cases



82% EP	RR = 2.70 [1.96-3.73]
77% Testosterone-like continuous	RR = 4.16 [2.56-6.75]
23% MPA cyclical	RR = 3.02 [1.8-5.05]
20% E only	RR = 1.96 [1.16-3.35]