

Diagnosis and Treatment of Patients with early and advanced Breast Cancer



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Gynecological Issues in Breast Cancer Patients

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- **Versions 2015–2020:**
**Albert / Bauerfeind / Blohmer/ Fersis / Gerber / Hanf / Huober/
Loibl / Maas / Rody / Scharl / Thill / Witzel**
- **Version 2021:**
Reimer / Thomssen

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Hormone (Replacement) Therapy (HT) of Estrogen Deficiency after Diagnosis of Breast Cancer



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	Oxford LoE	GR	AGO
<u>Systemic hormone (replacement-) therapy</u>			
▪ Endocrine responsive disease (ER pos.)	1b	B	-
▪ Combined treatment TAM plus low dose HT	2b	B	+/-
▪ Endocrine non-responsive disease (ER neg.)	2b	D	+/-
▪ Tibolone	1b	A	--
<u>Topical vaginal application of</u>			
▪ Estriol (E3 0.03 mg as treatment course*)	2b	B	+/-
▪ DHEA locally	2b	B	-
▪ Testosterone locally	2b	B	-
▪ Estradiol (E2) during AI therapy	4	C	-

* **4 weeks daily 1 x 1, followed by 8 weeks 3 x 1 per week** – Note: Elevated E3-blood levels only with start of therapy; oncological endpoints were not studied. Non-hormonal alternatives should be preferred, see slide „Sexual Health“

Further Medical Approaches to Reduce Menopausal Symptoms I

	Oxford		
	LoE	GR	AGO
Medical approaches* (reduction of hot flashes)			
▪ Selective serotonin reuptake inhibitors and serotonin-(noradrenalin) reuptake inhibitors (SSRI-SNRI): reduce hot flashes in BC patients			
▪ Venlafaxine	1a	A	+
▪ Desvenlafaxine	1b	A	+/-
▪ Sertraline, escitalopram	1b	A	+/-
▪ Gabapentin (patients using TAM)	1a	A	+
▪ Oxybutynine (2.5 mg/5 mg)	1b	A	+/-
▪ Pregabalin	1b	A	+/-
▪ Clonidine 0.05-0.15 mg/die (patients using TAM)	2a	B	+/-
▪ MPA (i.m. 500 mg single shot) (most potent, but endocrine agent!)	1b	A	+/-
▪ Vitamin E	1b	A	-
▪ Omega-3 fatty acids	1b	A	+/-
Medical approaches (other treatment goals)			
▪ Melatonin (improvement in sleep quality)	2b	C	+
▪ Duloxetine (treating arthralgia while on AI)	1b	B	+

*Note: Substantial placebo-effect has been proven (23-57%) **LoE 1b A +**

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CAM* - Approaches to Reduce Menopausal Symptoms II

* Complementary and Alternative Medicine

During anti-cancer treatment: Beware of drug interactions!

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> Soy-derived phytoestrogens – isoflavonoids* <ul style="list-style-type: none"> Hot flushes Sleep disturbance Topical vaginal application 	1b	B	-
	1b	B	+/-
	1b	B	+/-
<ul style="list-style-type: none"> Red Clover isoflavonoids* <ul style="list-style-type: none"> Hot flushes, sleep disturbance 	1b	B	+/-
<ul style="list-style-type: none"> Flaxseed-supplementation (40 g/d) (in HR+ ≤ 10 g/d) (reduces relapses, no effect on hot flushes) 	2b	B	+/-
<ul style="list-style-type: none"> Black Cohosh for hot flushes 	1b	B	+/-
<ul style="list-style-type: none"> Black cohosh + St. John's Wort (fixed combination) 	1b	B	+/-
<ul style="list-style-type: none"> St. John's Wort (pharmacokinetic interference with endocrine therapy, cytotoxic drugs, and tyrosin kinase inhibitors) 	1b	B	+/-
<ul style="list-style-type: none"> Ginseng root (Panax ginseng or P. quinquefolius) 	1b	B	-
<ul style="list-style-type: none"> Bromelain + Papain + Selenium + Lectin (for AI induced joint symptoms) 	3b	B	+
<ul style="list-style-type: none"> Homeopathic medicine to reduce hot flushes (consider placebo-effect) 	1b	B	+/-

* might stimulate BC, especially in endocrine responsive disease

General Approaches to Reduce Menopausal Symptoms III - Integrative Oncology Aspects

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General approaches:

- **Physical exercise**
- **Cognitive behavioral therapy (CBT), hypnosis**
- **Mind body-medicine
(yoga, education, counselling, mindfulness training)**

(Electro) Acupuncture

- **Aromatase-inhibitor treatment induced arthralgia**
- **Hot flushes**
- **Depression**
- **Anxiety, Sleep**

Oxford		
LoE	GR	AGO
1A	A	++
1a	A	++
1b	B	+
1b	B	+
1a	B	+/-
2b	B	+/-
3b	C	+/-

Ovarian Protection and Fertility Preservation in Premenopausal Patients Receiving (Neo)-Adjuvant Chemotherapy (CT)

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- **Fertility preservation counselling including referral of all potential patients to appropriate reproductive specialists (further information <https://fertiprotekt.com/english>)**
- **CTx + GnRHa (preservation of ovarian function) (GnRHa application > 2 weeks prior to chemotherapy, independent of hormone receptor status)**
- **CTx + GnRHa (preservation of fertility)**

Oxford		
LoE	GR	AGO
		++
1a	A	+
1b	A	+/-

Ovarian Protection – Synopsis of Randomized Trials

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	ZORO	PROMISE	Munster et al. - US	POEMS	Option
Patient number	60 (60 HR-)	281 (50 HR-)	49 (13 HR-) of 124	218 (218 HR-)	227 (126 HR-)
Age median	38 years	39 years	39 years	Premenop. < 50 years	premenopausal
Treatment	goserelin	triptorelin	triptorelin	goserelin	goserelin
Start of treatment	>2 weeks prior to cht	>1 week prior to cht	> 1 week prior to cht	> 1 week prior to cht	> 1 week prior to cht
Primary Endpoint	menstruation at month 6 after chemotherapy	rate of early menopause at month 12 after cht	menstruation rate within 2 years after cht	Ovarian failure at 2 yrs after cht	Amenorrhea with elevated FSH levels between 12 and 24 months
Primary objective	to detect 30% absolute increase of menstruation rate	to detect at least 20% absolute reduction in early menopause	to detect 20% difference in amenorrhea rate – from 10% to 30%		To detect 20%-25% absolute reduction in early menopause
Multivar. analysis	age as only independent predictive factor	treatment as only independent predictive factor	n.d.	Treatment as only independent predictive factor	Age, total cyclophosphamide dose and baseline AMH
Resumption of menses at month 12	83% with LHRH vs. 80% w/o	93% with LHRHa vs. 74% w/o	74% with LHRH vs. 68% w/o	78% with LHRH vs. 75% w/o; at 2 years; 22% with LHRH vs. 8%	78% with LHRHa vs. 62% amnorrhea rate between month 12 and 24
Median time to restoration of menses (months)	6.1 with LHRHa vs. 6.8 w/o; p=0.30	not reached with LHRH vs. 6.7 w/o; p=0.07	5.8 with LHRH vs. 5.0 w/o; p=0.58	n.d.	n.d.
Cyclophosph. dose	4600 vs. 4700mg	4080 vs. 4008 mg	n.r.	n.a.	5940 vs. 5940mg

Assessment of Ovarian Reserve

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Tests for fertility assessment

- **Anti-Mullerian Hormone**
- **Antral follicle count**
- **FSH**
- **Combined test procedures for assessment of ovarian reserve***

	Oxford		
	LoE	GR	AGO
1b	B	+	
3b	B	+	
2b ^a	B	+	
5	C	+	

* Tests are suggested for women > 35y and infertility for 6-12 months; the tests do not predict failure to conceive. They should be used in counselling patients and to provide a rough estimate of the fertility window. Results may decrease patient referral time to infertility centers.

Contraceptive Options for Women after Diagnosis of Breast Cancer

	Oxford		
	LoE	GR	AGO
■ Barrier methods	5	D	+
■ Sterilization (tubal ligation/salpingectomy/vasectomy)	5	D	+
■ Non-hormonal intrauterine devices (IUDs)	3b	D	+
■ Levonorgestrel-releasing IUDs	2b	C	-
■ Removal in newly diagnosed patients	4	D	+/-
■ Timing methods	5	D	-
■ Injectable progestin-only contraceptives	5	D	-
■ Progestin-only oral contraceptives	5	D	-
■ Combined oral contraceptives	5	D	-
■ Options of emergency contraception			
■ Copper intrauterine device (Copper-IUD)	5	D	+
■ Levonorgestrel, Ulipristal orally	5	D	+

- Barrier methods
- Sterilization (tubal ligation/salpingectomy/vasectomy)
- Non-hormonal intrauterine devices (IUDs)
- Levonorgestrel-releasing IUDs
 - Removal in newly diagnosed patients
- Timing methods
- Injectable progestin-only contraceptives
- Progestin-only oral contraceptives
- Combined oral contraceptives
- Options of emergency contraception
 - Copper intrauterine device (Copper-IUD)
 - Levonorgestrel, Ulipristal orally

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Sexual Health / Vaginal Dryness

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Evaluation

- **Assessment of sexual dysfunction**
- **Use of patient-reported questionnaires**

Therapy of dyspareunia and vaginal dryness

- **Psychoeducational support, group therapy, sexual counselling, marital counselling, psychotherapy**
- **Topical vaginal treatment**
 - **Non-hormonal lubricants /moisturizers** (also with physiotherapy)
 - **Estriol (E3 0.03 mg as treatment course*)**
 - **DHEA local application**
 - **Testosterone local application**
 - **Estradiol (E2) during AI therapy**
 - **Fractionated microablative CO₂-Laser/Vaginal Erbium:YAG-Laser**

	Oxford		
	LoE	GR	AGO
	5	D	+
	4	C	+
	1b	B	+
	1b	B	+
	2b	B	+/-
	2b	B	-
	2b	B	-
	4	C	-
	2a	B	+/-

* **4 weeks daily 1 x 1, followed by 8 weeks 3 x 1 per week** – Note:.. Elevated E3-blood levels only with start of therapy; oncological endpoints were not studied. **Non-hormonal alternatives should be preferred.**

Assessment of Sexual Health

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- **Brief Sexual Symptom Checklist (BSSC-W)^{ref2}**

- **Screening-Questionnaire: Overall Sexual Function**

1. Are you satisfied with your sexual life?	Yes - No
<i>If NO, please continue to question 2</i>	
2. How long have you been dissatisfied with your sexual life?
3. The problem(s) with your sexual life is:	<i>(mark one or more)</i>
1. Problem with little or no interest in sex	0
2. Problem with decreased genital sensation of clitoris or vagina (feeling)	0
3. Problem with decreased vaginal lubrication (dryness)	0
4. Problem reaching orgasm	0
5. Problem with pain and/or cramping during sex	0
6. Other
4. Which problem is most bothersome?	1 - 2 - 3 - 4 - 5 - 6 <i>(circle)</i>
5. Would you like to talk about it with your doctor?	Yes - No

- **Sexual Complaints Screener For Women (SCS-W)^{ref3}**

- **FSFI-19, FSFI-6^{ref5}**