

# Diagnosis and Treatment of Patients with early and advanced Breast Cancer



© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2019.1

## Gynecological Issues in Breast Cancer Patients

[www.ago-online.de](http://www.ago-online.de)

**FORSCHEN  
LEHREN  
HEILEN**

# Gynecologic Issues in Breast Cancer Patients

© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2019.1

- **Version 2015–2018:**  
**Albert / Bauerfeind / Fersis / Gerber / Hanf /  
Loibl / Maas / Scharl / Thill / Witzel**
- **Version 2019:**  
**Blohmer / Huober**

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

Oxford

- Endocrine responsive disease (ER pos.)
- Endocrine non-responsive disease (ER neg)
- Endocrine responsive disease (ER pos.): combined treatment TAM plus low-dose-HT
- Tibolone
- Topical vaginal application of
  - Estriol (E3 0.03 mg as treatment course\*)
  - Estradiol (E2) during AI therapy

LoE	GR	AGO
1b	B	-
2b	D	+/-
2b	B	+/-
1b	A	--
4	D	+/-
4	C	-

\* 4 weeks daily 1 x 1, followed by 8 weeks 3 x 1 per week

# Further Medical Approaches to Reduce Menopausal Symptoms I

© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2019.1

## Medical approaches:

- **Selective serotonin reuptake inhibitors and serotonin-(noradrenalin) reuptake inhibitors (SSRI-SNRI): reduce hot flashes in BC patients**
  - Venlafaxine
  - Desvenlafaxine
  - sertraline, escitalopram
- **Gabapentin (patients using TAM)**
- **Pregabalin**
- **Clonidine (patients using TAM)**
- **Oxybutynin (2,5mg/5 mg)**
- **MPA (i.m. 500 mg single shot)**  
(most potent, but endocrine agent!)
- **Vitamin E**
- **Omega 3 fatty acids**
- **Melatonin (improvement in sleep quality)**
- **Duloxetine (treating arthralgias while having an AI)**

Oxford		
LoE	GR	AGO

1a	A	+
1b	A	+/-
1b	A	+/-
1a	A	+
1b	A	+/-
1a <sup>a</sup>	A	+/-
1b	A	+/-
1b	A	-
1b	A	+/-
2b	C	+
1b	B	+

# CAM\* - Approaches to Reduce Menopausal Symptoms II

\* Complementary and Alternative Medicine

While anti-cancer treatment:

**Beware of drug interactions!**

- **Soy-derived phytoestrogens – isoflavonoids**

**Hot flush**

**Sleep disturbance**

**Topical vaginal application**

- **Red Clover isoflavonoids**

**Hot flush, sleep disturbance**

(might stimulate BC especially in endocrine responsive disease)

- **Flaxseed-supplementation (40 g/d) (in HR+ ≤ 10 g/d)**

**(reduces relapses, no effect on hot flashes)**

- **Black Cohosh for hot flushes**

- **Black cohosh + St. John's Wort**

- **St. John's Wort**

(pharmacokinetic interference with endocrine therapy, cytotoxic drugs and tyrosin kinase inhibitors)

- **Ginseng root (Panax ginseng or P. quinquefolius)**

- **Bromelain + Papain + Selenium + Lektin (for, AI induced joint symptoms)**

	Oxford		
	LoE	GR	AGO
Hot flush	1b	B	-
Sleep disturbance	1b	B	+/-
Topical vaginal application	1b	B	+/-
Hot flush, sleep disturbance (might stimulate BC especially in endocrine responsive disease)	1b	B	+/-
Flaxseed-supplementation (40 g/d) (in HR+ ≤ 10 g/d) (reduces relapses, no effect on hot flashes)	2b	B	+/-
Black Cohosh for hot flushes	1b	B	+/-
Black cohosh + St. John's Wort	1b	B	+/-
St. John's Wort (pharmacokinetic interference with endocrine therapy, cytotoxic drugs and tyrosin kinase inhibitors)	1b	B	+/-
Ginseng root (Panax ginseng or P. quinquefolius)	1b	B	-
Bromelain + Papain + Selenium + Lektin (for, AI induced joint symptoms)	3b	B	+

# General Approaches to Reduce Menopausal Symptoms III Integrative Oncology Aspects

© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2019.1

## General approaches:

- **Physical exercise**
  - **Mind body-medicine**  
(yoga, hypnosis, education, counseling)
  - **Cognitive behavioral therapy (CBT)**
  - **(Electro) Acupuncture**
- Aromatase-inhibitor treatment induced arthralgia**
- Hot flashes**
- Depression**
- Anxiety, Sleep**

Oxford		
LoE	GR	AGO
<b>1b</b>	<b>B</b>	<b>++</b>
<b>1b</b>	<b>B</b>	<b>+</b>
<b>1b</b>	<b>B</b>	<b>++</b>
<b>1b<sup>a</sup></b>	<b>B</b>	<b>+</b>
<b>1a</b>	<b>B</b>	<b>+/-</b>
<b>2b</b>	<b>B</b>	<b>+/-</b>
<b>3b</b>	<b>C</b>	<b>+/-</b>

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

© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2019.1

- **CT + GnRHa  
(preserve ovarian function)  
(GnRHa application > 2 weeks prior to chemotherapy, independently of hormone receptor status )**
- **CHT + GnRHa  
(preserve fertility)**
- **Fertility preservation counselling including referral of all potential patients to appropriate reproductive specialists (further information [www.fertiprotect.de](http://www.fertiprotect.de))**

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

# Ovarieller Funktionserhalt – Synopsis der randomisierten Studien

	ZORO	PROMISE	Munster et al. - US	POEMS	Option
<b>Patient number</b>	60 (60 HR-)	281 (50 HR-)	49 (13 HR-) of 124	218 (218 HR-)	227 (126 HR-)
<b>Age median</b>	38 years	39 years	39 years	Premenop. < 50 years	premenopausal
<b>Treatment</b>	goserelin	triptorelin	triptorelin	goserelin	goserelin
<b>Start of treatment</b>	>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
<b>Primary Endpoint</b>	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
<b>Primary objective</b>	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
<b>Multivar. analysis</b>	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
<b>Resumption of menses at month 12</b>	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% amenorrhea rate between month 12 and 24
<b>Median time to restoration of menses (months)</b>	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.
<b>Cyclophosph. dose</b>	4600 vs. 4700mg	4080 vs. 4008 mg	n.r.	n.a.	5940 vs. 5940mg

© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2019.1

www.ago-online.de

FORSCHEN  
LEHREN  
HEILEN



# Testing Ovarian Reserve

© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2019.1

## Assessment of ovarian reserve in infertile patients (> 6-12 months without conception)\*

### Tests for fertility assessment

- Anti-Müllerian Hormone
- Antral follicle count

Oxford		
LoE	GR	AGO
5	C	+
1b	B	+
3b	B	+

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

# Assessment of Ovarian Reserve

Tests recommended to assess ovarian reserved (according to ACOG Committee Opinion No. 618: Ovarian Reserve Testing. Obstetrics & Gynecology 2015;125: 268-273

Test	Details
FSH (follicle stimulating hormone) plus estradiol	<ul style="list-style-type: none"> <li>▪ Serum level on cycle day 2–3</li> <li>▪ Variation between cycles possible</li> <li>▪ High FSH value is associated with poor response to ovarian stimulation</li> </ul>
Anti Müllerian Hormone (AMH)	<ul style="list-style-type: none"> <li>▪ No specific timing for the test</li> <li>▪ Stable value within and between menstrual cycles</li> <li>▪ Low AMH value is associated with poor response to ovarian stimulation</li> </ul>
Antral follicle count (AFC)	<ul style="list-style-type: none"> <li>▪ Number of visible follicles (2–10 mm) during transvaginal ultrasound</li> <li>▪ Performed on cycle days 2–5</li> <li>▪ Number of antral follicles correlates with ovarian response to stimulation</li> </ul>

The tests do not predict failure to conceive. They should be used in counselling patients and 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



© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2019.1

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

www.ago-online.de

FORSCHEN  
LEHREN  
HEILEN

# Sexual Health

© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2019.1

	Oxford		
	LoE	GR	AGO
▪ Use of patient-reported questionnaires	4	C	+
▪ Assessment of sexual dysfunction	5	C	+
▪ Vaginal dryness: Non-hormonal lubricants / moisturizers	1b	B	+
▪ Fractionated microablative CO2-Laser/Vaginal Erbium:YAG-Laser	2b	B	+/-
▪ DHEA local application	1b	B	+/-
▪ Ospemifen (SERM)	1a	B	+/-
▪ Topical vaginal application of			
▪ Estriol (E3 0.03 mg as treatment course*) 4 D +/-	4	D	+/-
▪ Estradiol (E2) during AI therapy 4 D -	4	C	-
▪ Psychoeducational support, group therapy, sexual counseling, marital counseling, psychotherapy	1b	B	+

\* 4 weeks daily 1 x 1, followed by 8 weeks 3 x 1 per week

# Assessment of Sexual Health

© AGO e. V.  
in der DGGG e.V.  
sowie  
in der DKG e.V.

Guidelines Breast  
Version 2019.1

## ■ Sexual Complaints Screener (SCS) for women\*

German Translation

### Screening-Check-Fragebogen: Overall Sexual Function

1. Are you satisfied with your sexual life? yes, no; if no
2. How long have you been dissatisfied with your sexual life?
3. The problems with your sexual life are: (mark one or more):
  1. Problem with little or no interest in sex
  2. Problem with decreased genital sensation (feeling)
  3. Problem with decreased vaginal lubrication (dryness)
  4. Problem reaching orgasm
  5. Problem with pain during sex
  6. Other
4. Which problem is most bothersome? (circle) 1, 2, 3, 4, 5, 6.
5. Would you like to talk about it with your doctor?

\* Hatzichristou D, Rosen RC, Denogatis LR, Low WY, Sadovsky R, Symonds T. Recommendations for the clinical evaluation of men and women with sexual dysfunction. J Sex Med 2010;7:337-348