

# Diagnostik und Therapie primärer und metastasierter Mammakarzinome

## Gynäkologische Probleme bei Mammakarzinompatientinnen

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- **Version 2015-2017:**  
Albert / Bauerfeind / Fersis / Gerber / Hanf / Loibl / Scharl / Thill
- **Version 2018:**  
Maass / Witzel

## Screened data bases:

Pubmed	2009 –2017
ASCO	2009 - 2017
Cochrane	2009 - 2017
Medline	2009 - 2017

Screened:      Metaanalyses/ Systematic reviews / RCT / Cohort studies

# Hormon-(Ersatz-)Therapie (HT) für Östrogenmangelsymptome nach Mammakarzinom-Diagnose und -Therapie

	Oxford		
	LoE	GR	AGO
▪ Hormonsensitive Erkrankung (Rezeptor pos.)	1b	B	-
▪ Nicht-hormonsensitive Erkrankung (Rez. neg.)	3b	D	+/-
▪ Hormonsensitive Erkrankung (Rez. pos.): Kombinationstherapie: TAM plus niedrig dos. HT	2b	B	+/-
▪ Tibolon	1b	A	- -
▪ Topisch vaginale Applikation			
▪ Östriol (E3 0,03 mg als Kur*)	4	D	+/-
▪ Östradiol (E2) während einer AI-Therapie	4	C	-

\* Kur: 4 Wochen tägl. 1 x 1, dann 8 Wo lang 3 x 1 pro Woche

## Endocrine responsive disease

## Endocrine non-responsive disease

## Endocrine responsive disease: combined treatment TAM plus low-dose-HT

1. Holmberg L: Increased risk of recurrence after hormone replacement therapy in breast cancer survivors. J Natl Cancer Inst 100:475-82, 2008.
2. Fahlén M: Hormone replacement therapy after breast cancer: 10 year follow up of the Stockholm randomised trial. Eur J Cancer. 2013 Jan;49(1):52-9.
3. Lupo M, Dains JE, Madsen LT. Hormone Replacement Therapy: An Increased Risk of Recurrence and Mortality for Breast Cancer Patients? J Adv Pract Oncol. 2015 Jul-Aug;6(4):322-30. Epub 2015 Jul
4. Kuhle CL, Kapoor E, Sood R et al.: Menopausal hormone therapy in cancer survivors: A narrative review of the literature. Maturitas. 2016 Oct;92:86-96.

## Tibolone

1. Sismondi P, Kimmig R., Kubista E. et al.: Effects of Tibolone on climacteric symptoms and quality of life in breast cancer patients—Data from LIBERATE trial. Maturitas. 2011;70:365–372.
2. Bundred NJ: Tibolone increases bone mineral density but also relapse in breast cancer survivors: LIBERATE trial bone substudy. Breast Cancer Res. 2012 Jan 17;14(1):R13.

### Topical Vaginal Application

1. Biglia N, Peano E, Sgandurra P, et al. Low-dose vaginal estrogens or vaginal moisturizer in breast cancer survivors with urogenital atrophy: a preliminary study. *Gynecol Endocrinol* 2010;26(6):404–12
2. Le Ray I., Dell’Aniello S., Bonnetain F. et al.: Local estrogen therapy and risk of breast cancer recurrence among hormone treated patients: A nested case-control study. *Breast Cancer Res. Treat.* 2012;135:603–609.
3. Portman DJ, Gass ML; Vulvovaginal Atrophy Terminology Consensus Conference Panel. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and The North American Menopause Society. *Climacteric* 2014 Oct;17(5):557-63
4. Buchholz S, Mögele M, Lintermans A et al.: Vaginal estriol-lactobacilli combination and quality of life in endocrine-treated breast cancer. *Climacteric.* 2015;18(2):252-9.
5. Donders G, Belle G, Neven P et al.: Effect of ultra-low-dose estriol and lactobacilli vaginal tablets (Gynoflor®) on inflammatory and infectious markers of the vaginal ecosystem in postmenopausal women with breast cancer on aromatase inhibitors. *Eur J Clin Microbiol Infect Dis* (2015) 34:2023–2028
6. Cold S et al. Vaginal estrogens and risk of recurrence or death in women treated for estrogen receptor positive breast cancer, *European Journal of Cancer* 2015,51, S3 (Abstract)
7. Mazzaello S1, Hutton B, Ibrahim MF et al.: Management of urogenital atrophy in breast cancer patients: a systematic review of available evidence from randomized trials. *Breast Cancer Res Treat.* 2015 Jul;152(1):1-8. doi: 10.1007/s10549-015-3434-z. Epub 2015 May 24.
8. Melisko ME, Goldman ME, Hwang J et al. (2017): Vaginal testosterone cream vs estradiol vaginal ring for vaginal dryness or decreased libido in women receiving aromatase inhibitors for early-stage breast cancer: a randomized clinical trial. *JAMA Oncol.* 3(3):313-319.
9. American College of Obstetricians and Gynecologists’ Committee on Gynecologic Practice, Farrell R. ACOG Committee Opinion No. 659: The Use of Vaginal Estrogen in Women With a History of Estrogen-Dependent Breast Cancer. *Obstet Gynecol.* 2016 Mar;127(3):e93-6

## Weitere Methoden zur Erleichterung postmenopausaler Symptome nach Mamma-Ca I

### Medikamentöse Ansätze:

	Oxford		
	LoE	GR	AGO
■ <b>Selektive Serotonin-Reuptake-Inhibitoren und Serotonin-(Noradrenalin) Reuptake-Inhibitoren (SSRI-SNRI): zur Reduktion von Hitzewallungen</b>			
■ 1 <sup>ste</sup> Wahl: Venlafaxin	1a	A	+
■ 2 <sup>te</sup> Wahl: Desvenlafaxin	1b	A	+/-
■ 3 <sup>te</sup> Wahl: Sertralin, Escitalopram	1b	A	+/-
■ <b>Gabapentin (MaCa-Pat. unter Tamoxifen-Therapie)</b>	1a	A	+
■ <b>Pregabalin</b>	1b	A	+/-
■ <b>Clonidin (MaCa-Pat. unter Tamoxifen-Therapie)</b>	1a	A	+
■ <b>MPA (i.m. 500 mg als Einzeldosis)</b> (sehr wirksam, aber endokrin wirkende Substanz!)	1b	A	+/-
■ <b>Vitamin E</b>	1b	A	-
■ <b>Melatonin (verbesserte Schlafqualität)</b>	2b	C	+

1. Chubak J, Bowles EJ, Yu O, Buist DS et al.: Breast cancer recurrence in relation to antidepressant use. *Cancer Causes Control*. 2016 Jan;27(1):125-36.
2. Haque R, Shi J, Schottinger JE et al.: Tamoxifen and Antidepressant Drug Interaction in a Cohort of 16 887 Breast Cancer Survivors. *J Natl Cancer Inst*. 2015 Dec 1;108(3).
3. L'Espérance S: Pharmacological and non-hormonal treatment of hot flashes in breast cancer survivors: CEPO review and recommendations. *Support Care Cancer*. 2013 May;21(5):1461-74
4. Kelly CM, Juurlink DN, Gomes T et al. Selective serotonin reuptake inhibitors and breast cancer mortality in women receiving tamoxifen: a population based cohort study. *BMJ*. 2010;340:c693.
5. Bordeleau L: Multicenter, randomized, cross-over clinical trial of venlafaxine versus gabapentin for the management of hot flashes in breast cancer survivors. *J Clin Oncol*. 2010 Dec 10;28(35):5147-52.
6. Wiśniewska I, Jochymek B, Lenart-Lipińska M et al.: The pharmacological and hormonal therapy of hot flushes in breast cancer survivors. *Breast Cancer*. 2016 Mar;23(2):178-82.
7. Antoine C, Ameye L, Paesmans M et al.: Treatment of climacteric symptoms in breast cancer patients: a retrospective study from a medication databank. *Maturitas*. 2014 Jul;78(3):228-32.
8. Drewe J, Bucher KA, Zahner C. A systematic review of non-hormonal treatments of vasomotor symptoms in climacteric and cancer patients. *Springerplus*. 2015;10;4:65.

9. Leon-Ferre RA, Majithia N, Loprinzi CL. Management of hot flashes in women with breast cancer receiving ovarian function suppression. *Cancer Treat Rev*. 2017 Jan;52:82-90.

### SSRI

1. Shams T1, Firwana B, Habib F et al.: SSRIs for hot flashes: a systematic review and meta-analysis of randomized trials. *J Gen Intern Med*. 2014 Jan;29(1):204-13.

### Venlafaxine

1. Ramaswami R, Villarreal MD, Pitta DM et al.: Venlafaxine in management of hot flashes in women with breast cancer: a systematic review and meta-analysis. *Breast Cancer Res Treat*. 2015 Jul;152(2):231-7.
2. Boekhout AH, Vincent AD, Dalesio OB et al: Management of hot flashes in patients who have breast cancer with venlafaxine and clonidine: a randomized, double-blind, placebo-controlled trial. *J Clin Oncol*. 2011 Oct 10;29(29):3862-8.
3. Bordeleau L, Pritchard KI, Loprinzi CL et al: Multicenter, randomized, cross-over clinical trial of venlafaxine versus gabapentin for the management of hot flashes in breast cancer survivors. *J Clin Oncol*. 2010 Dec 10;28(35):5147-52.

### Desvenlafaxine

1. Archer DF, Dupont CM, Constantine GD et al.: Desvenlafaxine for the treatment of vasomotor symptoms associated with menopause: a double-blind, randomized, placebo-controlled trial of efficacy and safety. *Am J Obstet Gynecol*. 2009;200(3):238 e231–238 e210.
2. Speroff L, Gass M, Constantine G et al.: Efficacy and tolerability of desvenlafaxine succinate treatment for menopausal vasomotor symptoms: a randomized controlled trial. *Obstet Gynecol*. 2008;111(1):77–87.
3. Deecher DC, Alf inito PD, Leventhal L et al.: Alleviation of thermoregulatory dysfunction with the new serotonin and norepinephrine reuptake inhibitor desvenlafaxine succinate in ovariectomized rodent models. *Endocrinology*. 2007;148(3):1376–1383.

### Paroxetine

1. Simon JA, Portman DJ, Kaunitz AM et al.: Low-dose paroxetine 7.5 mg for menopausal vasomotor symptoms: two randomized controlled trials. *Menopause*. 2013 Oct;20(10):1027-35. doi: 10.1097/GME.0b013e3182a66aa7.

### Fluoxetine

1. Loprinzi CL, Sloan J, Stearns V et al.: Newer antidepressants and gabapentin for

hot flashes: an individual patient pooled analysis. J Clin Oncol. 2009;27(17):2831–2837.

#### Citalopram

1. Barton DL, LaVasseur B, Sloan JA et al.: A phase III trial evaluating three doses of citalopram for hot flashes: NCCTG trial N05C9. J Clin Oncol. 2008;26(20):9538.
2. Kalay AE, Demir B, Haberal A et al.: Efficacy of citalopram on climacteric symptoms. Menopause. 2007;14(2):223–229.

#### Gabapentin

1. Bordeleau L, Pritchard KI, Loprinzi CL et al: Multicenter, randomized, cross-over clinical trial of venlafaxine versus gabapentin for the management of hot flashes in breast cancer survivors. J Clin Oncol. 2010 Dec 10;28(35):5147-52

#### Pregabalin

1. Loprinzi CL, Qin R, Baclueva EP et al.: Phase III, randomized, double-blind, placebo-controlled evaluation of pregabalin for alleviating hot flashes, N07C1. J Clin Oncol. 2010;28(4):641–647.

#### Clonidin

1. Drewe J, Bucher KA, Zahner CA.: systematic review of non-hormonal treatments of vasomotor symptoms in climacteric and cancer patients. Springerplus. 2015 Feb 10;4:65. doi: 10.1186/s40064-015-0808-y. eCollection 2015.
2. Boekhout AH, Vincent AD, Dalesio OB et al: Management of hot flashes in patients who have breast cancer with venlafaxine and clonidine: a randomized, double-blind, placebo-controlled trial. J Clin Oncol. 2011 Oct 10;29(29):3862-8
3. Friedman GD, Udaltsova N, Habel LA: Norepinephrine antagonists and cancer risk. Int J Cancer 2011. 128(3):737–738, doi:10.1002/ijc.25351 (Clonidin)

#### (D) MPA (depo-) (Medroxyprogesterone acetate)

1. Prior JC, Nielsen JD, Hitchcock CL et al.: Medroxyprogesterone and conjugated oestrogen are equivalent for hot flushes: a 1-year randomized double-blind trial following premenopausal ovariectomy. Clin Sci (Lond). 2007;112(10):517–525.
2. Loprinzi CL, Levitt R, Barton D et al.: Phase III comparison of depomedroxyprogesterone acetate to venlafaxine for managing hot flashes: North Central Cancer Treatment Group Trial N99C7. J Clin Oncol. 2006 Mar 20;24(9):1409-14. Epub 2006 Feb 27.

#### Vitamine E

1. Rada G: Non-hormonal interventions for hot flushes in women with a history of breast cancer (Review). The Cochrane Library 2010, Issue 9.
2. Greenlee H, Hershman DL, Jacobson JS: Use of antioxidant supplements during breast cancer treatment: a comprehensive review. Breast Cancer Res Treat. 2009 Jun;115(3):437-52.
3. Biglia N, Sgandurra P, Peano E et al.: Non-hormonal treatment of hot flushes in breast cancer survivors: gabapentin vs. vitamin E. Climacteric. 2009 Aug;12(4):310-8.

### Melatonin

1. Chen WY, Giobbie-Hurder A, Gantman K et al.: A randomized, placebo-controlled trial of melatonin on breast cancer survivors: impact on sleep, mood, and hot flashes. Breast Cancer Res Treat 2014. 145(2):381–388, doi:10.1007/s10549-014-2944-4



# CAM\*-Therapie

## Postmenopausale Symptome II

\* Complementary and Alternative Medicine

Bei laufender onkologischer Standardtherapie:  
CAVE: Medikamenten-Interaktionen!

- **Soja – Isoflavonoide**  
Hitzewallungen  
Schlafstörungen  
topische vaginale Applikation
- **Rotklee – Isoflavonoide**  
Hitzewallungen und Schlafstörungen  
(Aktivierung von MaCa-Zellen insbes. bei hormon-rezeptorpositiver Erkrankung nicht ausgeschlossen)
- **Leinsamen (40 g/d)** (bei HR+ ≤ 10g/d (1Essl.))  
(mögl. Reduktion des Rezidivrisikos, keine Reduktion v. Hitzewallungen)
- **Traubensilberkerze gegen Hitzewallungen**  
Traubensilberkerze und Johanniskraut als fixe Kombi
- **Johanniskraut-Produkte**  
(cave: pharmakokinetische Interferenz mit endokriner Therapie, Zytostatika und Tyrosinkinase-Inhibitoren)
- **Ginseng Wurzel** (Panax ginseng or P. quinquefolius)
- **Bromelain + Papain + Selen + Lektin (AI-induzierte Gelenksbeschwerden)**

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

- Roberts H. Safety of herbal medicinal products in women with breast cancer. Maturitas. 2010;66(4):363-9.
- Ma H: Estrogenic botanical supplements, health-related quality of life, fatigue, and hormone-related symptoms in breast cancer survivors: a HEAL study report. BMC Complement Altern Med. 2011;11:109.
- Kim W, Lee WB, Lee JW et al.: Traditional herbal medicine as adjunctive therapy for breast cancer: A systematic review. Complement Ther Med. 2015 Aug;23(4):626-32. doi: 10.1016/j.ctim.2015.03.011.
- Lethaby A, Marjoribanks J, Kronenberg F et al.: Phytoestrogens for menopausal vasomotor symptoms. Cochrane Database Syst Rev. 2013 Dec 10;(12):CD001395. doi: 10.1002/14651858.CD001395.pub4.

### Soy- derieved isoflavonoids

### Red clover-derived isoflavonoids

- Chen MN: Efficacy of phytoestrogens for menopausal symptoms: a meta-analysis and systematic review. Climacteric. 2015 Apr;18(2):260-9.
- Lethaby A: Phytoestrogens for menopausal vasomotor symptoms. Cochrane Database Syst Rev. 2013 Dec 10;12:CD001395.
- Fritz H, Seely D, Flower G et al.: red clover, and isoflavones and breast cancer: a systematic review. PLoS One. 2013 Nov 28;8(11):e81968.
- Ghazanfarpour M, Sadeghi R, Latifnejad Roudsari R et al.: Effects of red clover on hot

flash and circulating hormone concentrations in menopausal women: a systematic review and meta-analysis. *Avicenna J Phytomed*. 2015 Nov-Dec;5(6):498-511.

5. Shakeri F: Effectiveness of red clover in alleviating of menopausal symptoms: A 12-week randomized, controlled trial. *Climacteric*. 2015;18(4):568-73.
6. Ghazanfarpour M, Latifnejad Roudsari R, Treglia G et al.: Topical administration of isoflavones for treatment of vaginal symptoms in postmenopausal women: A systematic review of randomised controlled trials. *J Obstet Gynaecol*. 2015 Nov;35(8):783-7.
7. Ghazanfarpour M, Sadeghi R, Roudsari RL. The application of soy isoflavones for subjective symptoms and objective signs of vaginal atrophy in menopause: A systematic review of randomised controlled trials. *J Obstet Gynaecol*. 2016;36(2):160-71.

#### Flaxseed

1. Flower G: Flax and Breast Cancer: A Systematic Review. *Integr Cancer Ther*. 2013 8;13(3):181-192.
2. Pruthi S: A phase III, randomized, placebo-controlled, double-blind trial of flaxseed for the treatment of hot flashes: North Central Cancer Treatment Group N08C7. *Menopause* 2012; 19:48-53.

#### Black cohosh (*Cimicifuga racemosa*) nor St John's Wort nor Ginseng root

1. Leach MJ: Black cohosh (*Cimicifuga* spp.) for menopausal symptoms. *Cochrane Database Syst Rev*. 2012; 9:CD007244.
2. Caraci F: Metabolic drug interactions between antidepressants and anticancer drugs: focus on selective serotonin reuptake inhibitors and hypericum extract. *Curr Drug Metab*. 2011 Jul 1;12(6):570-7.
3. Kim MS: Ginseng for managing menopause symptoms: a systematic review of randomized clinical trials. *J Ginseng Res*. 2013 Mar;37(1):30-6.

#### Sodium selenite, proteolytic plant enzymes (bromelain and papain), and *Lens culinaris* lectin

1. Beuth J, van Leendert R, Schneider B et al.: Complementary medicine on side-effects of adjuvant hormone therapy in patients with breast cancer. *In Vivo*. 2013 Nov-Dec;27(6):869-71.

# Postmenopausale Symptome III integrativ-onkologische Therapien

## Allgemeine Ansätze:

- **Körperliches Training / Sport**
- **Mind Body-Medizin**  
(Yoga, Hypnose, Schulung, Beratung)
- **Kognitive Verhaltenstherapie**
- **Akupunktur**  
Aromatase-Inhibitor induzierte Arthralgie  
Hitzewallungen  
Depressionen  
Angst, Schlafstörungen

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

1. Duncan M, Moschopoulou E, Herrington E et al.: Review of systematic reviews of non-pharmacological interventions to improve quality of life in cancer survivors. BMJ Open. 2017 Nov 28;7(11):e015860. doi: 10.1136/bmjopen-2017-015860.

### Physical exercise

1. Duijts SF: Efficacy of cognitive behavioral therapy and physical exercise in alleviating treatment-induced menopausal symptoms in patients with breast cancer: results of a randomized, controlled, multicenter trial. J Clin Oncol. 2012 Nov 20;30(33):4124-33.

2. Hartman SJ, Nelson SH, Myers E et al.: Randomized controlled trial of increasing physical activity on objectively measured and self-reported cognitive functioning among breast cancer survivors: The memory & motion study. Cancer. 2018 Jan 1;124(1):192-202. doi: 10.1002/cncr.30987. Epub 2017 Sep 19.

### Mind Body Medicine

1. Mann E: Cognitive behavioural treatment for women who have menopausal symptoms after breast cancer treatment (MENOS 1): a randomised controlled trial. Lancet Oncol. 2012 Mar;13(3):309-18.

2. Buffart LM: Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials. BMC Cancer. 2012 Nov 27;12:559.

3. Cramer H: Characteristics of randomized controlled trials of yoga: a bibliometric

analysis. BMC Complement Altern Med. 2014 Sep 2;14:328.

4. Koch AK, Rabsilber S, Lauche R et al.: The effects of yoga and self-esteem on menopausal symptoms and quality of life in breast cancer survivors-A secondary analysis of a randomized controlled trial. *Maturitas* 2017 Nov;105:95-99. doi: 10.1016/j.maturitas.2017.05.008. Epub 2017 May 13.
5. Goldstein KM, Shepherd-Banigan M, Coeytaux RR et al.: Use of mindfulness, meditation and relaxation to treat vasomotor symptoms. *Climacteric*. 2017;20(2):178-82.
6. Stefanopoulou E, Grunfeld EA. Mind-body interventions for vasomotor symptoms in healthy menopausal women and breast cancer survivors. A systematic review. *J Psychosom Obstet Gynaecol*. 2017;38(3):210-25
7. Tao WW, Tao XM, Song CL. Effects of non-pharmacological supportive care for hot flushes in breast cancer: a meta-analysis. *Support Care Cancer*. 2017;25(7):2335-47

#### Cognitive behavioral therapy

1. Mewes JC, Steuten LM, Duijts SF et al.: Cost-effectiveness of cognitive behavioral therapy and physical exercise for alleviating treatment-induced menopausal symptoms in breast cancer patients. *J Cancer Surviv*. 2015 Mar;9(1):126-35. doi: 10.1007/s11764-014-0396-9. Epub 2014 Sep 2.
2. Desautels C, Savard J, Ivers H et al.: Treatment of Depressive Symptoms in Patients with Breast Cancer: A Randomized Controlled Trial Comparing Cognitive Therapy and Bright Light Therapy. *Health Psychol*. 2017 Nov 27. doi: 10.1037/hea0000539. [Epub ahead of print]

#### Acupuncture

1. Chiu HY1, Shyu YK, Chang PC et al.: Effects of Acupuncture on Menopause-Related Symptoms in Breast Cancer Survivors: A Meta-analysis of Randomized Controlled Trials. *Cancer Nurs*. 2016 May-Jun;39(3):228-37.
2. Garland SN1, Xie SX, Li Q et al.: Comparative effectiveness of electro-acupuncture versus gabapentin for sleep disturbances in breast cancer survivors with hot flashes: a randomized trial. *Menopause*. 2017 May;24(5):517-523. doi: 10.1097/GME.0000000000000779.
3. Chen L, Lin CC, Huang TW et al.: Effect of acupuncture on aromatase inhibitor-induced arthralgia in patients with breast cancer: A meta-analysis of randomized controlled trials. *Breast*. 2017;33:132-8.
4. Chien TJ, Hsu CH, Liu CY et al.: Effect of acupuncture on hot flush and menopause symptoms in breast cancer- A systematic review and meta-analysis. *PLoS One*. 2017;12(8):e0180918.
5. Hershman DL, Unger JM, Greenlee H et al.: Randomized blinded sham- and waitlist-controlled trial of acupuncture for joint symptoms related to aromatase inhibitors in women with early stage breast cancer (S1200). *San Antonio Breast*



## Prophylaxe des ovariellen Funktionsausfalls und Fertilitätserhaltung bei prämenopausalen Patientinnen mit (neo-)adjuvanter Chemotherapie (CT)

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li>■ CHT + GnRHa (zur Prophylaxe des ovariellen Funktionsausfalls) (GnRHa Applikation &gt; 2 Wochen vor Chemotherapie, unabhängig vom Hormonrezeptorstatus)</li> </ul>	1a	B	+
<ul style="list-style-type: none"> <li>■ CHT + GnRHa (zur Erhöhung der Schwangerschaftsrate)</li> </ul>	2a	B	+/-
<ul style="list-style-type: none"> <li>■ Angebot zur Beratung über Fertilitätserhaltung</li> </ul>	4	C	++
<ul style="list-style-type: none"> <li>■ Fertilitätserhalt mit assist. reprod. Therapie (Information: <a href="http://www.fertiprotect.de">www.fertiprotect.de</a>)</li> </ul>	4	C	+

### Ovarian function protection

1. Gerber B, von Minckwitz G, Stehle H et al.: Effect of luteinizing hormone-releasing hormone agonist on ovarian function after modern adjuvant breast cancer chemotherapy: the GBG 37 ZORO study. J Clin Oncol. 2011 Jun 10;29(17):2334-41.
2. Del Mastro L, Ceppi M, Poggio F et al.: Gonadotropin-releasing hormone analogues for the prevention of chemotherapy-induced premature ovarian failure in cancer women: systematic review and meta-analysis of randomized trials. Cancer Treat Rev. 2014 Jun;40(5):675-83.
3. Del Mastro L, Rossi G, Lambertini M et al.: New insights on the role of luteinizing hormone releasing hormone agonists in premenopausal early breast cancer patients. Cancer Treat Rev. 2016 Jan;42:18-23.
4. Munholz RR, et al: Gonadotropin-Releaseing hormone agonists for ovarian function preservation in premenopausal women undergoing chemotherapy for early stage breast cancer- A systematic Review and Meta Analysis. JAMA Oncol 2016;2:65-73
5. Munster PN, Moore AP, Ismail-Khan R et al.: Randomized Trial Using Gonadotropin-Releasing Hormone Agonist Triptorelin for the Preservation of Ovarian Function During (Neo)Adjuvant Chemotherapy for Breast Cancer. J Clin Oncol. 2012;30(5):533–8.
6. Lambertini M, Boni L, Michelotti A et al.: Ovarian Suppression With Triptorelin During Adjuvant Breast Cancer Chemotherapy and Long-term Ovarian Function, Pregnancies, and Disease-Free Survival: A Randomized Clinical Trial. JAMA. 2015 Dec 22-29;314(24):2632-40. doi: 10.1001/jama.2015.17291.

7. Elgindy E, Sibai H, Abdelghani A et al.: Protecting Ovaries During Chemotherapy Through Gonad Suppression: A Systematic Review and Meta-analysis. *Obstet Gynecol.* 2015;126(1):187–95.
8. Sun X, Dongol S, Jiang J et al.: Protection of ovarian function by GnRH agonists during chemotherapy: a meta-analysis. *Int J Oncol.* 2014;44(4):1335–40.

#### Pregnancy rates

1. Lambertini M, Ceppi M, Poggio F et al.: Ovarian suppression using luteinizing hormone-releasing hormone agonists during chemotherapy to preserve ovarian function and fertility of breast cancer patients: a meta-analysis of randomized studies. *Ann Oncol* 2015; 26(12):2408-19.
2. Moore HCF, Unger JM, Phillips K-A et al. Goserelin for ovarian protection during breast-cancer adjuvant chemotherapy. *N Engl J Med.* 2015;372(10):923–32.
3. Lambertini M, Boni L, Michelotti A et al. Ovarian suppression with triptorelin during adjuvant breast cancer chemotherapy and long-term ovarian function, pregnancies, and disease-free survival. A randomized clinical trial. *JAMA.* 2015;314(24):2632-40.

#### Fertility preservation counselling

1. Loren AW, Mangu PB, Beck LN et al. Fertility Preservation for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol.* 2013;31(19):2500–10.
2. Peccatori FA, Azim Jr HA, Orecchia R et al. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2013;24 Suppl 6:vi160–70.
3. Abe A, Kuwahara A, Iwasa T et al.: A survey on fertility management in young women of reproductive age treated with chemotherapy. *Int J Clin Oncol.* 2016 Dec;21(6):1183-1190.

#### Fertility preservation with assisted reproduction therapy

1. Dittrich R, Hackl J, Lotz L et al.: Pregnancies and live births after 20 transplantations of cryopreserved ovarian tissue in a single center. *Fertil Steril.* 2015 Feb;103(2):462-8.
2. Gamzatova Z, Komlichenko E, Kostareva A et al.: Autotransplantation of cryopreserved ovarian tissue--effective method of fertility preservation in cancer patients. *Gynecol Endocrinol.* 2014 Oct;30 Suppl 1:43-7.
3. Luke B, Brown MB, Missmer SA et al.: Assisted reproductive technology use and outcomes among women with a history of cancer. *Hum Reprod.* 2016 Jan;31(1):183-9.
4. Goldrat O, Kroman N, Peccatori FA et al.: Pregnancy following breast cancer using assisted reproduction and its effect on long-term outcome. *Eur J Cancer.*

2015;51(12):1490–6.

5. Oktay K, Turan V, Bedoschi G et al.: Fertility Preservation Success Subsequent to Concurrent Aromatase Inhibitor Treatment and Ovarian Stimulation in Women With Breast Cancer. *J Clin Oncol*. 2015;33(22):2424–9.



# 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% amnorrhea 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

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# Testung der ovariellen Reserve

## Einschätzung der ovariellen Reserve (> 6-12 Monate ohne Konzeption)\*

### Tests zur Fertilitäts-Beurteilung

- Anti-Müller Hormon
- Antrale Follikelzählung

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

\* Tests werden vorgeschlagen für Frauen > 35 J und Kinderwunsch für 6-12 Monate; die Tests präzisieren nicht den Misserfolg einer Konzeption, aber helfen über das potenziell verkürzte Zeitfenster für eine erfolgreiche Konzeption aufzuklären und über die Möglichkeiten einer Infertilitätsbehandlungen aufzuklären.

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# Abschätzung der ovariellen 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>

All the tests do not predict failure to conceive, but they allow to counsel that the window of opportunity to conceive may be shorter than anticipated.

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

# Kontrazeptive Möglichkeiten für Brustkrebspatientinnen

	Oxford		
	LoE	GR	AGO
■ <b>Barriere-Methoden</b>	5	D	+
■ <b>Sterilisation (Tubenligatur / Vasektomie)</b>	5	D	+
■ <b>Nicht-hormonelle intrauterine devices (IUDs)</b>	3b	D	+
■ <b>Levonorgestrel-freisetzende IUDs</b>	2b	C	-
■ Entfernung bei Erstdiagnose	4	D	+/-
■ <b>Timing-Methoden</b>	5	D	-
■ <b>Reine Progesteron-Kontrazeptiva (oral / i.m.)</b>	5	D	-
■ <b>Komb. orale Kontrazeptiva</b>	5	D	-
■ <b>Optionen für Notfall-Kontrazeption für Frauen nach Brustkrebs</b>			
■ Kupfer armierte Intrauterin-Devices (Cu-IUD)	5	D	+
■ Levonorgestrel, Ulipristalacetat oral	5	D	+

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## Emergency Contraception - Options after Diagnosis of Breast Cancer

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# Sexuelle Gesundheit

- Tests zur Beurteilung sexueller Dysfunktion
- Nutzung von Patientinnenfragebögen
- Vaginale Trockenheit  
Nicht-hormonelle Gleitmittel / Feuchtgele
- Fraktionierter mikroablativer CO<sub>2</sub>-Laser/  
vaginaler Erbium:YAG-Laser
- Psychoedukative Unterstützung,  
Gruppentherapie, Sexualberatung,  
Eheberatung, Psychotherapie

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

1. Runowicz CD1, Leach CR2, Henry NL1 et al.: American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline. J Clin Oncol. 2015 Dec 7. pii: JCO.2015.64.3809

## Vaginal dryness

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2. Advani P, Brewster AM, Baum GP et al.: A pilot randomized trial to prevent sexual dysfunction in postmenopausal breast cancer survivors starting adjuvant aromatase inhibitor therapy. J Cancer Surviv. 2017;11(4):477-85
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## Laser therapy

1. Salvatore S, Pitsouni E, Del Deo F et al.: Sexual Function in Women Suffering From Genitourinary Syndrome of Menopause Treated With Fractionated CO<sub>2</sub> Laser. Sex Med Rev. 2017;5(4):486-94
2. Gambacciani M, Levancini M. Vaginal erbium laser as second-generation

thermotherapy for the genitourinary syndrome of menopause: a pilot study in breast cancer survivors. *Menopause*. 2017;24(3):316-9.

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# Tests zur sexuellen Gesundheit

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

German Translation

### Screening-Check-Fragebogen: Sexuelle Gesundheit

1. Sind Sie zufrieden mit Ihrem Sexualleben? Ja, nein, wenn nein
2. Seit wann/wie lange sind Sie mit Ihrem Sexualleben unzufrieden?
3. Ihr Problem im Sexualleben ist:
  1. Kein Interesse bzw. keine Lust
  2. Reduzierte Empfindlichkeit/Sensibilität im Genitalbereich
  3. Trockenheit der Scheide
  4. Problem, den Orgasmus zu erreichen
  5. Schmerzen beim Geschlechtsverkehr
  6. Andere
4. Welche Probleme stören Sie am meisten? 1, 2, 3, 4, 5, 6.
5. Wollen Sie über diese Probleme mit Ihrem Arzt/Ihrer Ärztin reden?

\* 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

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