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Guidelines Breast
Version 2021.1D

FORSCHEN
LEHREN
HEILEN

Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Gynäkologische Probleme bei Mammakarzinompatientinnen



Gynäkologische Probleme bei Mammakarzinompatientinnen

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

Screened data bases:

Pubmed	2009 –2020
ASCO	2009 - 2020
SABCS	2009 - 2020

Übersichten:

1. Marsh S, Borges VF, Coons HL, Afghahi A. Sexual health after a breast cancer diagnosis in young women: clinical implications for patients and providers. Breast Cancer Res Treat. 2020 Dec;184(3):655-663.
2. ESHRE Guideline Group on Female Fertility Preservation, Anderson RA, Amant F, Braat D et al. ESHRE guideline: female fertility preservation. Hum Reprod Open. 2020 Nov 14;2020(4):hoaa052.
3. Lambertini M, Peccatori FA, Demeestere I et al.; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Fertility preservation and post-treatment pregnancies in post-pubertal cancer patients: ESMO Clinical Practice Guidelines[†]. Ann Oncol. 2020 Dec;31(12):1664-1678. S3

4. The North American Menopause Society (NAMS). The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society. Menopause. 2020 Sep;27(9):976-992.
5. S3-Leitlinie: Peri- and Postmenopause. Diagnosis and Interventions. Guideline of the DGGG, SGGG and OEGGG (S3 Level, AWMF Registry No.015-062, January 2020). <http://www.awmf.org/leitlinien/detail/II/015-062.html>

Screened: Metaanalyses/ Systematic reviews / RCT / Cohort studies

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

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

* Kur: 4 Wo. tägl. 1 x 1, dann 8 Wo lang 3 x 1 pro Wo. - Anm. Außer zu Beginn kein E3-Übertritt in das Blut; onkologische Endpunkte nicht geprüft.
 Nicht-hormonelle Alternativen sind zu bevorzugen, siehe Folie „Sexuelle Gesundheit / Vaginale Trockenheit“

Endocrine responsive disease

1. 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.
2. Holmberg L: Increased risk of recurrence after hormone replacement therapy in breast cancer survivors. J Natl Cancer Inst 100:475-82, 2008.
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. Mudhune GH, Armour M, McBride KA: Safety of menopausal hormone therapy in breast cancer survivors older than fifty at diagnosis: A systematic review and meta-analysis. Breast 2019, 47:43-55.
5. Wang Y, Lewin N, Qaoud Y et al. The oncologic impact of hormone replacement therapy in premenopausal breast cancer survivors: A systematic review. Breast. 2018 Aug;40:123-130. doi: 10.1016/j.breast.2018.05.002. Epub 2018 May 12.

Endocrine non-responsive disease

1. Wang Y, Lewin N, Qaoud Y et al. The oncologic impact of hormone replacement therapy in premenopausal breast cancer survivors: A systematic review. *Breast*. 2018 Aug;40:123-130. doi: 10.1016/j.breast.2018.05.002. Epub 2018 May 12.

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

1. 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. Kenemans P, Bundred NJ, Foidart J et al.; LIBERATE Study Group. Safety and efficacy of tibolone in breast-cancer patients with vasomotor symptoms: a double-blind, randomised, non-inferiority trial. *Lancet Oncol*. 2009 Feb;10(2):135-46.
2. 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.
3. 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.

Ospemifeme

1. Goldstein SR, Bachmann GA, Koninckx P et al.; Ospemifene Study Group. Ospemifene 12-month safety and efficacy in postmenopausal women with vulvar and vaginal atrophy. *Climacteric*. 2014 Apr;17(2):173-82.
2. Cagnacci A, Xholli A, Venier M. Ospemifene in the Management of Vulvar and Vaginal Atrophy: Focus on the Assessment of Patient Acceptability and Ease of Use. *Patient Prefer Adherence*. 2020 Jan 10;14:55-62.

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. Mazzarello 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.
7. 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
8. Melisko ME, Goldman ME, Hwang J et al. 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.* 2017; 3(3):313-319.
9. Barton DL, Shuster LT, Dockter T et al. Systemic and local effects of vaginal dehydroepiandrosterone (DHEA): NCCTG N10C1 (Alliance). *Support Care Cancer.* 2018 Apr;26(4):1335-1343.
10. Simon JA, Goldstein I, Kim NN et al. The role of androgens in the treatment of genitourinary syndrome of menopause (GSM): International Society for the Study of Women's Sexual Health (ISSWSH) expert consensus panel review. *Menopause.* 2018 Jul;25(7):837-847.
11. Villa P, Tagliaferri V, Amar ID et al. Local ultra-low-dose estriol gel treatment of vulvo-vaginal atrophy: efficacy and safety of long-term treatment. *Gynecol Endocrinol.* 2020 Jun;36(6):535-539.

12. The North American Menopause Society (NAMS). The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society. *Menopause*. 2020 Sep;27(9):976-992.
13. Jain AL, Jamy O, Mullins J et al. Usefulness of patient-reported outcomes to assess the effectiveness of topical hormonal therapy for gynecologic symptoms after antihormonal treatment for breast cancer. *Proc (Bayl Univ Med Cent)*. 2020 Apr 7;33(3):331-335.
14. Hirschberg AL, Sánchez-Rovira P, Presa-Lorite J et al. Efficacy and safety of ultra-low dose 0.005% estriol vaginal gel for the treatment of vulvovaginal atrophy in postmenopausal women with early breast cancer treated with nonsteroidal aromatase inhibitors: a phase II, randomized, double-blind, placebo-controlled trial. *Menopause*. 2020 May;27(5):526-534.

Weitere Methoden zur Erleichterung postmenopausaler Symptome nach Mamma-Ca

	Oxford		
	LoE	GR	AGO
Medikamentöse Ansätze* (Reduktion von Hitzewallungen):			
■ Selektive Serotonin-Reuptake-Inhibitoren und Serotonin-(Noradrenalin) Reuptake-Inhibitoren (SSRI-SNRI):			
■ Venlafaxin	1a	A	+
■ Desvenlafaxin	1b	A	+/-
■ Sertralin, Citalopram	1b	A	+/-
■ Gabapentin (MaCa-Pat. unter Tamoxifen-Therapie)	1a	A	+
■ Oxybutynin (2,5 mg/5 mg)	1b	A	+/-
■ Pregabalin	1b	A	+/-
■ Clonidin 0,05-0,15 mg/die (MaCa-Pat. unter Tamoxifen-Therapie)	2a	B	+/-
■ MPA (i.m. 500 mg single shot, wirksam, aber endokrin aktiv)	1b	A	+/-
■ Vitamin E	1b	A	-
■ Omega-3 Fettsäuren	1b	A	+/-
Medikamentöse Ansätze (andere Therapieziele):			
■ Melatonin (verbesserte Schlafqualität)	2b	C	+
■ Duloxetine (zur Therapie von Arthralgien nur unter AI-Therapie)	1b	B	+
*Beachte: Substanzieller Placebo-Effekt nachgewiesen (23-57%) LoE 1b A +			

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
2. Shan D, Zou L, Liu X, Shen Y, Cai Y, Zhang J. Efficacy and safety of gabapentin and pregabalin in patients with vasomotor symptoms: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2020 Jun;222(6):564-579.e12.

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)
4. **Burbos N, Morris EP. Menopausal symptoms. BMJ Clin Evid. 2011 Jun 15;2011:0804.**

Oxybutynin

1. **Leon-Ferre RA, Novotny PJ, Wolfe EG et al. Oxybutynin vs Placebo for Hot Flashes in Women With or Without Breast Cancer: A Randomized, Double-Blind Clinical Trial (ACCRU SC-1603). JNCI Cancer Spectr. 2019 Oct 21;4(1):pkz088.**
2. **Simon JA, Gaines T, LaGuardia KD; Extended-Release Oxybutynin Therapy for VMS Study Group. Extended-release oxybutynin therapy for vasomotor symptoms in women: a randomized clinical trial. Menopause. 2016 Nov;23(11):1214-1221.**

(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.

3. Ertz-Archambault NM, Rogoff LB, Kosiorek HE et al.: Depomedroxyprogesterone acetate therapy for hot flashes in survivors of breast cancer: no unfavorable impact on recurrence and survival. Support Care Cancer. 2019 Aug 11. doi: 10.1007/s00520-019-05013-7. [Epub ahead of print]

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.

Omega 3-Fettsäuren

1. Lustberg M'B, Orchard TS, Reinbolt R et al. Randomized placebo-controlled pilot trial of omega 3 fatty acids for prevention of aromatase inhibitor-induced musculoskeletal pain. Breast Cancer Res Treat. 2018 Feb;167(3) 709-718. doi: 10.1007/s10549-017-4559-z. Epub 2017 Nov 3.

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

Duloxetine

1. Henry NL, Unger JM, Schott AF et al. Randomized, Multicenter, Placebo-Controlled Clinical Trial of Duloxetine Versus Placebo for Aromatase Inhibitor-Associated Arthralgias in Early-Stage Breast Cancer: SWOG S1202. J Clin Oncol. 2018 Feb 1;36(4):326-332. doi: 10.1200/JCO.2017.74.6651. Epub 2017 Nov 14.

CAM*-Therapie Postmenopausale Symptome II

* Complementary and Alternative Medicine

Bei laufender onkologischer Standardtherapie: CAVE: Medikamenten-Interaktionen!	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ▪ Soja – Isoflavonoide* <ul style="list-style-type: none"> Hitzewallungen Schlafstörungen Topische vaginale Applikation 	1b 1b 1b	B B B	- +/- +/-
<ul style="list-style-type: none"> ▪ Rotklee – Isoflavonoide* <ul style="list-style-type: none"> Hitzewallungen und Schlafstörungen 	1b	B	+/-
<ul style="list-style-type: none"> ▪ Leinsamen (40 g/d) (bei HR+ ≤ 10g/d (1Essl.)) (mögl. Reduktion des Rezidivrisikos, keine Reduktion v. Hitzewallungen) 	2b	B	+/-
<ul style="list-style-type: none"> ▪ Traubensilberkerze gegen Hitzewallungen 	1b	B	+/-
<ul style="list-style-type: none"> ▪ Traubensilberkerze und Johanniskraut als fixe Kombi 	1b	B	+/-
<ul style="list-style-type: none"> ▪ Johanniskraut-Produkte (Cave: Pharmakokinetische Interferenz mit endokriner Therapie, Zytostatika und Tyrosinkinase-Inhibitoren) 	1b	B	+/-
<ul style="list-style-type: none"> ▪ Ginseng Wurzel (Panax ginseng or P. quinquefolius) 	1b	B	-
<ul style="list-style-type: none"> ▪ Bromelain + Papain + Selen + Lektin (AI-induzierte Gelenksbeschwerden) 	3b	B	+
<ul style="list-style-type: none"> ▪ Homöopathische Mittel zur Reduktion Hitzewallungen (Placebo-Effekt bedenken) 	1b	B	+/-

* Aktivierung von MaCa-Zellen bei HR-positiver Erkrankung nicht ausgeschlossen

1. Roberts H. Safety of herbal medicinal products in women with breast cancer. Maturitas. 2010;66(4):363-9.
2. 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.
3. 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.
4. 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

1. Chen MN: Efficacy of phytoestrogens for menopausal symptoms: a meta-analysis and systematic

review. *Climacteric*. 2015 Apr;18(2):260-9.

2. Lethaby A: Phytoestrogens for menopausal vasomotor symptoms. *Cochrane Database Syst Rev*. 2013 Dec 10;12:CD001395.
3. 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.
4. 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.
8. Ribeiro AE, Monteiro NES, Moraes AVG et al. Can the use of probiotics in association with isoflavone improve the symptoms of genitourinary syndrome of menopause? Results from a randomized controlled trial. *Menopause*. 2018 Dec 10. doi: 10.1097/GME.0000000000001279. [Epub ahead of print]

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.
4. Mehrpooya M1, Rabiee S2, Larki-Harchegani A3, Fallahian AM1, Moradi A4, Ataei S1, Javad MT5. A comparative study on the effect of "black cohosh" and "evening primrose oil" on menopausal hot flashes. J Educ Health Promot. 2018 Mar 1;7:36. doi: 10.4103/jehp.jehp_81_17. eCollection 2018.
5. **Wobser RW, Takov V. Black Cohosh. 2020 Dec 5. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan—. PMID: 29261886.**

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.

Homeopathic medicine

1. Heudel PE, Van Praagh-Doreau I, Duvert B et al.: Does a homeopathic medicine reduce hot flushes induced by adjuvant endocrine therapy in localized breast cancer patients? A multicenter randomized placebo-controlled phase III trial. Support Care Cancer. 2019 May;27(5):1879-1889. doi: 10.1007/s00520-018-4449-x. Epub 2018 Sep 7.

Postmenopausale Symptome III Integrativ-onkologische Therapien

Allgemeine Ansätze:

- Körperliches Training / Sport
- Kognitive Verhaltenstherapie, Hypnose
- Mind Body-Medizin
(Yoga, Schulung, Beratung, Achtsamkeitstraining)

(Elektro-) Akupunktur

- Aromatase-Inhibitor induzierte Arthralgie
- Hitzewallungen
- Depressionen
- Angst, Schlafstörungen

Oxford		
LoE	GR	AGO
1a	A	++
1a	A	++
1b	B	+
1b	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.
2. Tran S, Hickey M, Saunders C et al. Nonpharmacological therapies for the management of menopausal vasomotor symptoms in breast cancer survivors. Support Care Cancer. 2020 Sep 17. doi: 10.1007/s00520-020-05754-w. Epub ahead of print. PMID: 32940768.
3. S3-Leitlinie: Peri- und Postmenopause. Diagnosis and Interventions. Guideline of the DGGG, SGGG and OEGGG (S3 Level, AWMF Registry No.015-062, January 2020).
<http://www.awmf.org/leitlinien/detail/II/015-062.html>

Physical exercise

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Ovarschutz und Fertilitätserhaltung bei prämenopausalen Patientinnen mit (neo-)adjuvanter Chemotherapie (CT)

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ▪ Angebot zur Beratung über Fertilitätserhaltung inkl. assistierter Reproduktion (Information: https://fertiprotekt.com) 			++
<ul style="list-style-type: none"> ▪ CTx + GnRHa (zur Prophylaxe des ovariellen Funktionsausfalls) (GnRHa Applikation > 2 Wochen vor Chemotherapie, unabhängig vom Hormonrezeptorstatus) 	1a	A	+
<ul style="list-style-type: none"> ▪ CTx + GnRHa (zur Erhöhung der Schwangerschaftsrate) 	1b	A	+/-

Ovarian function protection

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Pregnancy rates

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Fertility preservation counselling

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Ovarian Protection – Synopsis of Randomized Trials

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sowie
in der DKG e.V.

Guidelines Breast
Version 2021.1D

	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% amenorrhea 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

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FORSCHEN
LEBEN
HEILEN

1. Munhoz RR, Pereira AA, Sasse AD et al.: Gonadotropin-Releasing 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 Jan 1;2(1):65-73.
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Einschätzung der ovariellen Reserve

	Oxford		
	LoE	GR	AGO
Tests zur Beurteilung der ovariellen Reserve			
▪ Anti-Müller Hormon	1b	B	+
▪ Antrale Follikelzählung	3b	B	+
▪ FSH	2b ^a	B	+
▪ Kombinierte Testverfahren zur Einschätzung der ovariellen Reserve*	5	C	+

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

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Antrale Follicle Count

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FSH

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Kontrazeptive Möglichkeiten für Brustkrebspatientinnen

	Oxford		
	LoE	GR	AGO
■ Barriere-Methoden	5	D	+
■ Sterilisation (Tubenligatur/Salpingektomie/Vasektomie)	5	D	+
■ Nicht-hormonelle intrauterine Devices (IUDs)	3b	D	+
■ Levonorgestrel-freisetzende IUDs	2b	C	-
■ Entfernung bei Erstdiagnose	4	D	+/-
■ Timing-Methoden	5	D	-
■ Reine Progesteron-Kontrazeptiva (oral / i.m.)	5	D	-
■ Kombinierte orale Kontrazeptiva	5	D	-
■ Optionen für Notfall-Kontrazeption			
■ 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 / Vaginale Trockenheit

Evaluation

- Einschätzung des sexuellen Beschwerdebildes
- Nutzung von Patientinnenfragebögen

Behandlung der Dyspareunie und der vaginalen Trockenheit

- Psychoedukative Unterstützung, Gruppentherapie, Sexualberatung, Eheberatung, Psychotherapie
- Vaginale / topische Behandlung
 - Nicht-hormonelle Vaginalgele (auch kombiniert mit Physioth.)
 - Östriol (E3 0,03 mg als Kur*)
 - DHEA lokal
 - Testosteron lokal
 - Östradiol (E2) während einer AI-Therapie
 - Fraktionierter mikroablativer CO₂-Laser / vag. 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	+/-

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

Anm. Außer zu Beginn kein E3-Übertritt in das Blut; onkologische Endpunkte nicht geprüft. Nicht-hormonelle Alternativen sind zu bevorzugen.

Übersichten:

1. The North American Menopause Society (NAMS). The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society. Menopause. 2020 Sep;27(9):976-992.
2. Runowicz CD, Leach CR, Henry NL 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

Evaluation

1. Sexual Complaints Screener For Women (SCS-W) (Langversion und Kurzversion):
2. Hatzichristou D, Rosen RC, Denogatis LR et al.: Recommendations for the clinical evaluation of men and women with sexual dysfunction. J Sex Med 2010;7:337-348
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4. Female Sexual Function Index (FSFI-19, FSFI-6):

5. Rosen R, Brown C, Heiman J et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther. 2000 Apr-Jun;26(2):191-208.
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Behandlung der Dyspareunie und der vaginalen Trockenheit

Psychoedukative Unterstützung, Gruppentherapie, Sexualberatung, Eheberatung, Psychotherapie

1. Carroll AJ, Baron SR, Carroll RA. Couple-based treatment for sexual problems following breast cancer: A review and synthesis of the literature. Support Care Cancer. 2016 Aug;24(8):3651-9.

Kombinationstherapie (Olivenöl, Beckenbodenentspannung und vaginale Feuchtigkeitsgele):

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Vaginal topische Behandlung

Medikamentös (nicht-hormonelle Vaginalgele, Östrogene, DHEA, Testosteron)

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
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Laser therapy

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FORSCHEN
LEBEN
HEILEN

Einschätzung der sexuellen Gesundheit

- **Kurze Checkliste Sexueller Symptome für Frauen (BSSC-W)^{ref2}**
 - **Screening-Fragebogen zur Sexualfunktion insgesamt**

1. Sind Sie zufrieden mit Ihrem Sexualleben? *Ja – Nein*

Wenn nein, dann beantworten Sie bitte die nächsten Fragen:

2. Seit wann/wie lange sind Sie mit Ihrem Sexualleben unzufrieden?

3a. Ihr Problem im Sexualleben ist: *(eins oder mehrere markieren)*

1. Problem mit weniger oder gar kein Interesse bzw. Lust	0
2. Problem mit reduzierter Empfindlichkeit / Sensibilität im Genitalbereich (Gefühl)	0
3. Problem mit verringerter vaginaler Lubrikation (Trockenheit der Scheide)	0
4. Problem, einen Orgasmus zu erreichen	0
5. Probleme mit Schmerzen beim Geschlechtsverkehr	0
6. Andere Probleme oder Sorgen

3b. Welche Probleme stören Sie am meisten? *Bitte ankreuzen: 1 – 2 – 3 – 4 – 5 – 6*

4. Wollen Sie über diese Probleme mit Ihrem Arzt/Ihrer Ärztin reden? *Ja – Nein*

- **Sexual Complaints Screener For Women (SCS-W)^{ref3,4}**
- **FSFI-19, FSFI-6^{ref5,6}**

General recommendations

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