Guidelines Breast
Version 2024.1D

FORSCHEN
LEHREN
HEILEN

Gynäkologische Probleme bei Mammakarzinompatientinnen

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- **Versionen 2015–2023:**
  Albert / Bauerfeind / Blohmer / Fehm / Fersis / Gerber / Hanf / Huober/ Loibl / Maas / Mundhenke /Reimer / Rody / Scharl / Stickeler/ Thill / Thomssen / Witzel
- **Version 2024:**
  Huober / Mundhenke

Screened data bases:

Pubmed	2009 –2023
ASCO	2009 - 2023
SABCS	2009 - 2023

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

	Oxford LoE	Oxford GR	AGO
Systemische Hormon-(Ersatz-)Therapie			
▪ **Hormonsensitive Erkrankung (ER pos.)**	1a	B	-
▪ **Kombinationstherapie: TAM plus niedrig dos. HT**	2b	B	+/-
▪ **Nicht-hormonsensitive Erkrankung (ER neg.)**	1a	B	+/-
▪ **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. Paggio F, Del Mastro L, Bruzzone M et al. Safety of systemic hormone replacemt therapy in breast cancer survivors: a systematic review and meta-analysis. Breast Cancer Res Treat. 2022 191(2):269-72.

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.
6. Luo J, Cochrane B B, Wactawski-Wende J. Effects of menopausal hormone therapy on ductal carcinoma in situ of the breast. Breast Cancer Res Treat. 2013;137:915–925.

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 Athrophy 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.

15. Hussain I, Sinai V, Talaulikar S. A systematic review of randomised clinical trials – The safety of vaginal hormones and selective estrogen receptor modulators for the treatment of genitourinary menopausal symptoms in breast cancer survivors. Post Reproductive Health 2023, Vol. 29(4) 222–23
16. Fallah P, Wolfe D, Hutton P et al. Management of genitourinary symptoms in patients with breast cancer: an updated systematic review of available evidence from randomized trials. Supportive Care in Cancer 2023 31:131
17. Merlino L, D`Matys V et al. Ovidio G, Therapeutic Choices for Genitourinary Syndrome of Menopause (GSM) in Breast Cancer Survivors: A Systematic Review and Update. Pharmaceuticals 2023, 16, 550.

Weitere Methoden zur Erleichterung post-menopausaler Symptome nach Mamma-Ca I

Medikamentöse Ansätze* (Reduktion von Hitzewallungen):	Oxford LoE	Oxford GR	AGO
▪ **Selektive Serotonin-Reuptake-Inhibitoren und Serotonin-(Noradrenalin) Reuptake-Inhibitoren (SSRI-SNRI):**			
▪ **Venlafaxin**	1a	A	+
▪ **Desvenlafaxin, 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	+/-
▪ **Omega-3 Fettsäuren**	1b	A	+/-
▪ **Vitamin E**	1b	A	-
Medikamentöse Ansätze (andere Therapieziele):			
▪ **Melatonin (verbesserte Schlafqualität)**	2b	C	+
▪ **Duloxetin (zur Therapie von Arthralgien nur unter AI-Therapie)**	1b	B	+

* *Beachte: Substantieller 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, et al. 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.

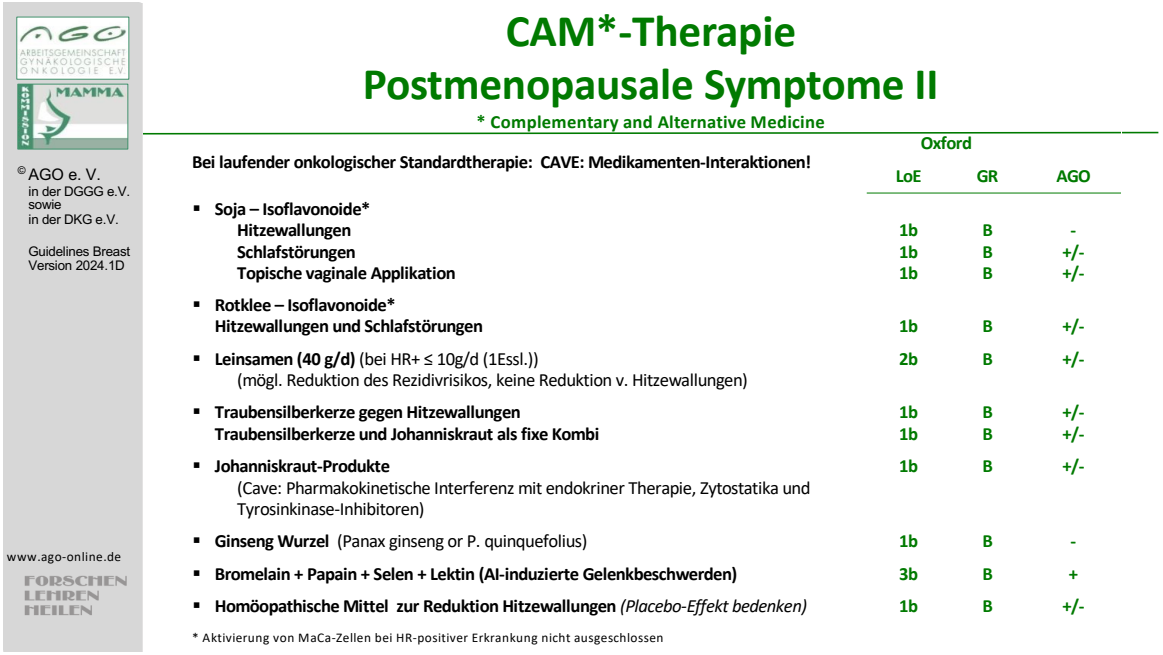
Melatonin

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

Duloxetin

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.



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.

<u>Soy- derieved isoflavonoids</u>

<u>Red clover-derived isoflavonoids</u>

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 (bromelaine 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:	Oxford LoE	Oxford GR	AGO
▪ Körperliches Training / Sport	1a	A	++
▪ Kognitive Verhaltenstherapie, Hypnose	1a	A	++
▪ Mind Body-Medizin (Yoga, Schulung, Beratung, Achtsamkeitstraining)	1b	B	+
▪ Kurzzeitige Pause der endokrinen Therapie bei inakzeptablen Nebenwirkungen statt Abbruch*	5	D	+
(Elektro-) Akupunktur			
▪ Aromatase-Inhibitor induzierte Arthralgie	1a	B	+
▪ Hitzewallungen	2a	B	+
▪ Angst, Depressionen	2b	B	+
▪ Schlafstörungen	2a	C	+

* Analog der SOLE-Studie

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- 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/ll/015-062.html

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.
3. Lahart IM, Metsios GS, Nevill AM et al.: Physical activity for women with breast cancer after adjuvant therapy. Cochrane Database Syst Rev 2018, 1:Cd011292.

Mind Body Medicine

1. 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.
2. Cramer H: Characteristics of randomized controlled trials of yoga: a bibliometric analysis. BMC Complement Altern Med. 2014 Sep 2;14:328.
3. Haller H, Winkler MM, Klose P et al.: Mindfulness-based interventions for women with breast cancer: an updated systematic review and meta-analysis. Acta Oncol 2017, 56:1665-76.
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
8. 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.

Cognitive behavioral therapy, Hypnosis

1. 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]
2. 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.
3. 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.

4. van Driel CM, Stuursma A, Schroevers MJ et al. Mindfulness, cognitive behavioural and behaviour-based therapy for natural and treatment-induced menopausal symptoms: a systematic review and meta-analysis. BJOG. 2019 Feb;126(3):330-339.
5. 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.

Acupuncture

1. Befus D, Coeytaux RR, Goldstein KM et al. Management of Menopause Symptoms with Acupuncture: An Umbrella Systematic Review and Meta-Analysis. J Altern Complement Med. 2018 Apr;24(4):314-323. doi: 10.1089/acm.2016.0408. Epub 2018 Jan 3.
2. 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.
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. 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.
6. Hershman DL, Unger JM, Greenlee H et al.: Effect of Acupuncture vs Sham Acupuncture or Waitlist Control on Joint Pain Related to Aromatase Inhibitors Among Women With Early-Stage Breast Cancer: A Randomized Clinical Trial. Jama 2018, 320:167-76
7. Wang W, Liu Y, Sun S et al. Electroacupuncture for postmenopausal women with stress urinary incontinence: secondary analysis of a randomized controlled trial. World J Urol. 2018 Oct 13. doi: 10.1007/s00345-018-2521-2. [Epub ahead of print]
8. 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.

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

	Oxford		
	LoE	GR	AGO
▪ **CTx + GnRHa (zur Prophylaxe des ovariellen Funktionsausfalls) (GnRHa Applikation > 2 Wochen vor Chemotherapie, unabhängig vom Hormonrezeptorstatus)**	1a	A	+
▪ **CTx + GnRHa (zur Erhöhung der Schwangerschaftsrate)**	2a	B	+/-
▪ **Angebot zur Beratung über Fertilitätserhalt inkl. assistierter Reproduktion (ART) (Information: *https://fertiprotekt.com; S2k-Leitlinie Fertilitätserhalt bei onkologischen Erkrankungen*)**			++

<u>Ovarian function protection</u>

1. 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.
2. 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
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 Dec 22-29;314(24):2632-40. doi: 10.1001/jama.2015.17291.
4. Lambertini M, Moore HCF, Leonard RCF et al.: Gonadotropin-Releasing Hormone Agonists During Chemotherapy for Preservation of Ovarian Function and Fertility in Premenopausal Patients With Early Breast Cancer: A Systematic Review and Meta-Analysis of Individual Patient-Level Data. J Clin Oncol 2018, 36:1981-90
5. Lambertini M, Boni L, Michelotti A et al.; GIM study group. Long-Term Outcomes With Pharmacological Ovarian Suppression During Chemotherapy in Premenopausal Early Breast Cancer Patients. J Natl Cancer Inst. 2022;114(3):400-408.
6. Zong X, Yu Y, Yang H, Chen W et al. Effects of Gonadotropin-Releasing Hormone Analogs on Ovarian Function Against Chemotherapy-Induced Gonadotoxic Effects in Premenopausal Women With Breast Cancer in China: A Randomized Clinical Trial. JAMA Oncol. 2022;8(2):252-258

7. Zong X, Yu Y, Chen W, Zong W, Yang H, Chen X. Ovarian reserve in premenopausal women with breast cancer. Breast. 2022;64:143-150
8. Li ZY, Dong YL, Cao XZ, Ren SS, Zhang Z. Gonadotropin-releasing hormone agonists for ovarian protection during breast cancer chemotherapy: a systematic review and meta-analysis. Menopause. 2022;29(9):1093-1100

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.
4. Lambertini M, Boni L, Michelotti A et al.; GIM study group. Long-Term Outcomes With Pharmacological Ovarian Suppression During Chemotherapy in Premenopausal Early Breast Cancer Patients. J Natl Cancer Inst. 2022;114(3):400-408.

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.
4. Marklund A, et al. Reproductive Outcomes After Breast Cancer in Women With vs Without Fertility Preservation. JAMA Oncol. 2021 Jan 1;7(1):86-91.
5. https://register.awmf.org/assets/guidelines/015-082l_S2k_Fertilitaetserhaltung-bei-onkologischen-Therapien_2017-12-verlaengert.pdf

Fertilitätsprotektion und assistierte Reproduktion

- Onkologische Sicherheit[1]-

	Oxford LoE	Oxford GR	AGO
▪ **Methoden des Fertilitätserhalt vor Therapie**			
GnRH-Analogon	1a	A	++
Kryokonservierung Ovargewebe mit anschliessender Transplantation[2]	4	D	+
Kryokonservierung Oozyten (unbefruchtet / befruchtet) nach ovarieller Stimulation	2a	C	+
▪ **Assistierte Reproduktion nach Mammakarzinom**	4	C	+/-

[1] Evidenzlage z.T. eingeschränkt auf Grund der Studienlage (keine prospektiv randomisierten Studien möglich)
[2] Risiko durch Tumorzellverschleppung bei Transplantation des Gewebes; bei Mutationsträgerinnen komplette Explantation des Transplantats nach Schwangerschaft notwendig

GnRH-Analogon:

1. Lambertini M, Moore HCF, Leonard RCF, et al. Gonadotropin-Releasing Hormone Agonists During Chemotherapy for Preservation of Ovarian Function and Fertility in Premenopausal Patients With Early Breast Cancer: A Systematic Review and Meta-Analysis of Individual Patient-Level Data. J Clin Oncol. 2018;36(19):1981-1990.
2. Lambertini M, Boni L, Michelotti A, et al. ; GIM study group. Long-Term Outcomes With Pharmacological Ovarian Suppression During Chemotherapy in Premenopausal Early Breast Cancer Patients. J Natl Cancer Inst. 2022;114(3):400-408. doi: 10.1093/jnci/djab213. PMID: 34850043; PMCID: PMC8902441.

Cryopreservation of ovarian tissue:

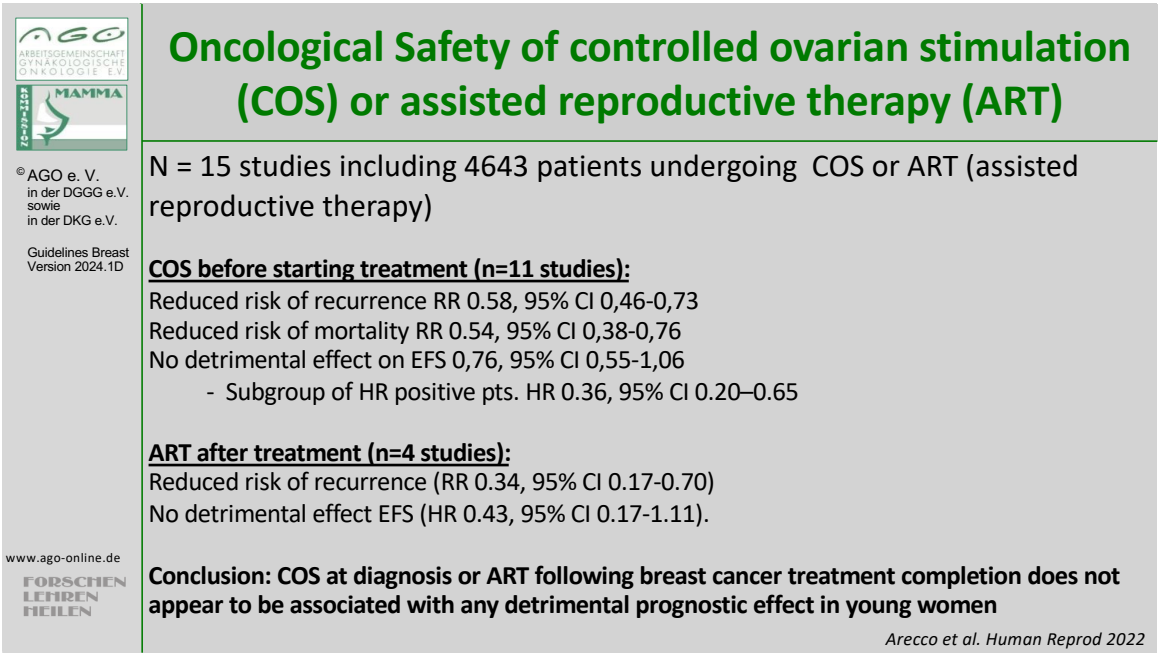
1. Bastings L, Beerendonk CC, Westphal JR, et al. Autotransplantation of cryopreserved ovarian tissue in cancer survivors and the risk of reintroducing malignancy: a systematic review. Hum Reprod Update. 2013;19(5):483-506. doi: 10.1093/humupd/dmt020. Epub 2013 Jun 30. PMID: 23817363.
2. Rosendahl M, Greve T, Andersen CY. The safety of transplanting cryopreserved ovarian tissue in cancer patients: a review of the literature. J Assist Reprod Genet. 2013;30(1):11-24. doi: 10.1007/s10815-012-9912-x. Epub 2012 Dec 22. PMID: 23263841; PMCID: PMC3553351.

Cryoconservation of oocytes after ovarian stimulation:

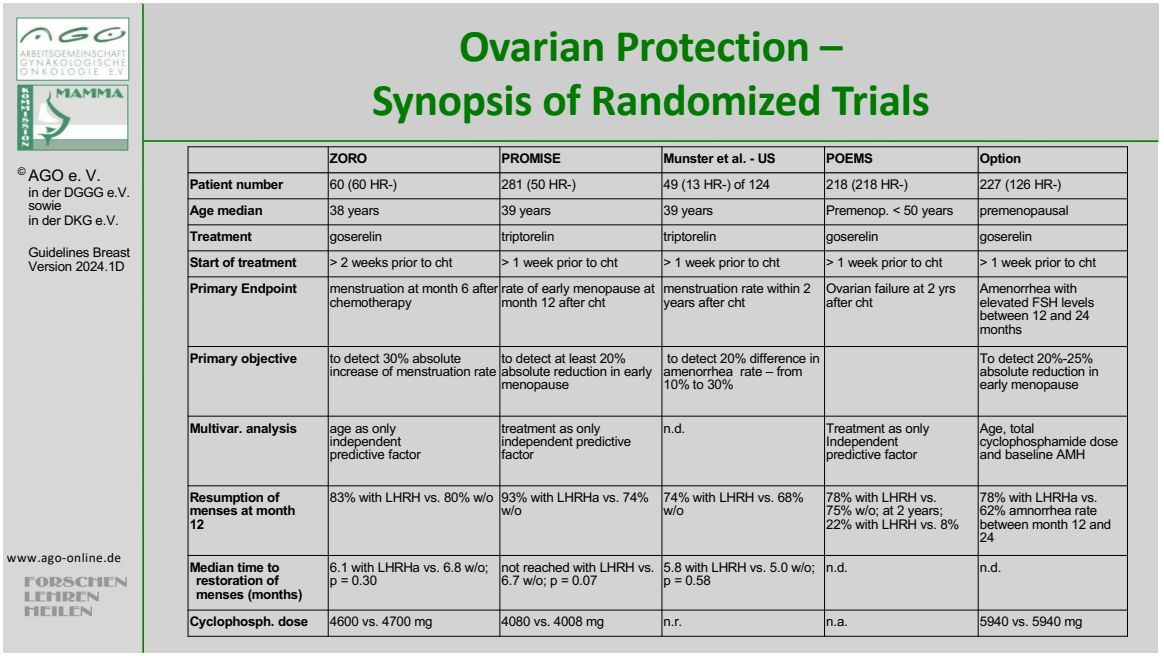
1. Luke B, Brown MB, Missmer SA et al.: Assisted reproductive technology use and outcomes among women with a history of cancer. Hum Reprod. 2016 ;31(1):183-9.
2. Oktay K, Turan V, Bedoschi G et al.: Fertility Preservation Success Subsequent to Concurrent Aromatase Inhibitor Treatment and Ovarian Stimulation in Women With Breast Cancer. J Clin Oncol. 2015;33(22):2424–9.
3. Arecco L, Blondeaux E, Bruzzone M, et al.. Safety of fertility preservation techniques before and after anticancer treatments in young women with breast cancer: a systematic review and meta-analysis. Hum Reprod. 2022; 37(5):954-968. doi: 10.1093/humrep/deac035. PMID: 35220429; PMCID: PMC9071231.
4. Rodgers RJ, Reid GD, Koch J, Deans R, et al. The safety and efficacy of controlled ovarian hyperstimulation for fertility preservation in women with early breast cancer: a systematic review. Hum Reprod. 2017;32(5):1033-1045. doi: 10.1093/humrep/dex027. PMID: 28333356.
5. Beebeejaun Y, Athithan A, Copeland TP, et al. Risk of breast cancer in women treated with ovarian stimulation drugs for infertility: a systematic review and meta-analysis. Fertil Steril. 2021; 116(1):198-207. doi: 10.1016/j.fertnstert.2021.01.044. PMID: 34148584.

ART after diagnosis of breast cancer:

1. Arecco L, Blondeaux E, Bruzzone M, et al.. Safety of fertility preservation techniques before and after anticancer treatments in young women with breast cancer: a systematic review and meta-analysis. Hum Reprod. 2022; 37(5):954-968. doi: 10.1093/humrep/deac035. PMID: 35220429; PMCID: PMC9071231.
2. Azim H, Niman S, Patridge A et al. Fertility preservation and assisted reproductive technologies in breast cancer pstien ts interrupting adjuvant endocrine therapy to attempt pregnancy. Results from the positive trial. SABCS 2023



1. Arecco L, Blondeaux E, Bruzzone M, et al.. Safety of fertility preservation techniques before and after anticancer treatments in young women with breast cancer: a systematic review and meta-analysis. Hum Reprod. 2022 ;37(5):954-968. doi: 10.1093/humrep/deac035. PMID: 35220429; PMCID: PMC9071231.



Ovarian Protection – Synopsis of Randomized Trials

	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. 4700 mg	4080 vs. 4008 mg	n.r.	n.a.	5940 vs. 5940 mg

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.
2. 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.
3. Del Mastro L, Boni L, Michelotti A et al. Effect of the gonadotropin-releasing hormone analogue triptorelin on the occurrence of chemotherapy-induced early menopause in premenopausal women with breast cancer: a randomized trial. JAMA. 2011 Jul 20;306(3):269-76.
4. 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.
5. 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.
6. Leonard RCF, Adamson DJA, Bertelli G et al.: GnRH agonist for protection against ovarian toxicity during chemotherapy for early breast cancer: the Anglo Celtic Group OPTION trial. Ann Oncol. 2017 Aug 1;28(8):1811-1816. doi: 10.1093/annonc/mdx184.
7. Lambertini M, Boni L, Michelotti A et al.; GIM study group. Long-Term Outcomes With Pharmacological Ovarian Suppression During Chemotherapy in Premenopausal Early Breast Cancer Patients. J Natl Cancer Inst. 2022;114(3):400-408.

Einschätzung der ovariellen Reserve

	Oxford LoE	Oxford 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**	**+**
Geringere ovarielle Reserve bei BRCAmt	**2b**	**B**	

* **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.**

AMH:

1. Anderson RA, Mansi J, Coleman RE et al.: The utility of anti-Müllerian hormone in the diagnosis and prediction of loss of ovarian function following chemotherapy for early breast cancer. Eur J Cancer. 2017;87:58-64
2. Fréour T, Barrière P, Masson D. Anti-müllerian hormone levels and evolution in women of reproductive age with breast cancer treated with chemotherapy. Eur J Cancer. 2017 Mar;74:1-8. doi: 10.1016/j.ejca.2016.12.008. Epub 2017 Jan 28.
3. Trapp E, Steidl J, Rack B et al.: Anti-Müllerian hormone (AMH) levels in premenopausal breast cancer patients treated with taxane-based adjuvant chemotherapy - A translational research project of the SUCCESS A study. Breast. 2017 Oct;35:130-135. doi: 10.1016/j.breast.2017.07.007. Epub 2017 Jul 18.
4. Morarji K, McArdle O, Hui K et al.: Ovarian function after chemotherapy in young breast cancer survivors. Curr Oncol. 2017 Dec;24(6):e494-e502. doi: 10.3747/co.24.3335. Epub 2017 Dec 20.
5. Zong X, Yu Y, Chen W, Zong W, Yang H, Chen X. Ovarian reserve in premenopausal women with breast cancer. Breast. 2022:143-150. doi: 10.1016/j.breast.2022.05.009.

Antrale Follicle Count:

1. Sinha N, Letourneau JM, Wald K et al: Antral follicle count recovery in women with menses after treatment with and without gonadotropin-releasing hormone agonist use during chemotherapy for breast cancer. J Assist Reprod Genet 2018, 35:1861-8.

2. Su HI, Chung K, Sammel MD et al.: Antral follicle count provides additive information to hormone measures for determining ovarian function in breast cancer survivors. Fertil Steril. 2011 Apr;95(5):1857-9.

FSH:

1. Furlanetto J, Thode C, Huober J. et al. Changes in hormone levels (E2, FSH, AMH) and fertility of young women treated with neoadjuvant chemotherapy (CT) for early breast cancer (EBC). SABCS 2017, # 754, PD 7-09
2. Furlanetto J, Marmé F, Seiler S, et al. Chemotherapy-induced ovarian failure in young women with early breast cancer: Prospective analysis of four randomised neoadjuvant/adjuvant breast cancer trials. Eur J Cancer. 2021;152:193-203. doi: 10.1016/j.ejca.2021.04.038.

Combined tests:

1. Practice Committee of the American Society for Reproductive Medicine. Electronic address: asrm@asrm.org; Practice Committee of the American Society for Reproductive Medicine. Testing and interpreting measures of ovarian reserve: a committee opinion. Fertil Steril. 2020;114(6):1151-1157

Ovarian reserve BRCA mt:

1. Zhang X, NiuJ, Che T et al. Fertility preservation in BRCA mutation carriers—efficacy and safety issues: a review
2. Reproductive Biology and Endocrinology 2020 18:11
3. Oktay KH, Volkan T, Bedoschi G et al. A prospective longitudinal analysis of the predictors of amenorrhea after breast cancer chemotherapy: Impact of *BRCA* pathogenic variants. *Cancer Medicine.* 2023;12:19225–19233.

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	+

Contraception (general)

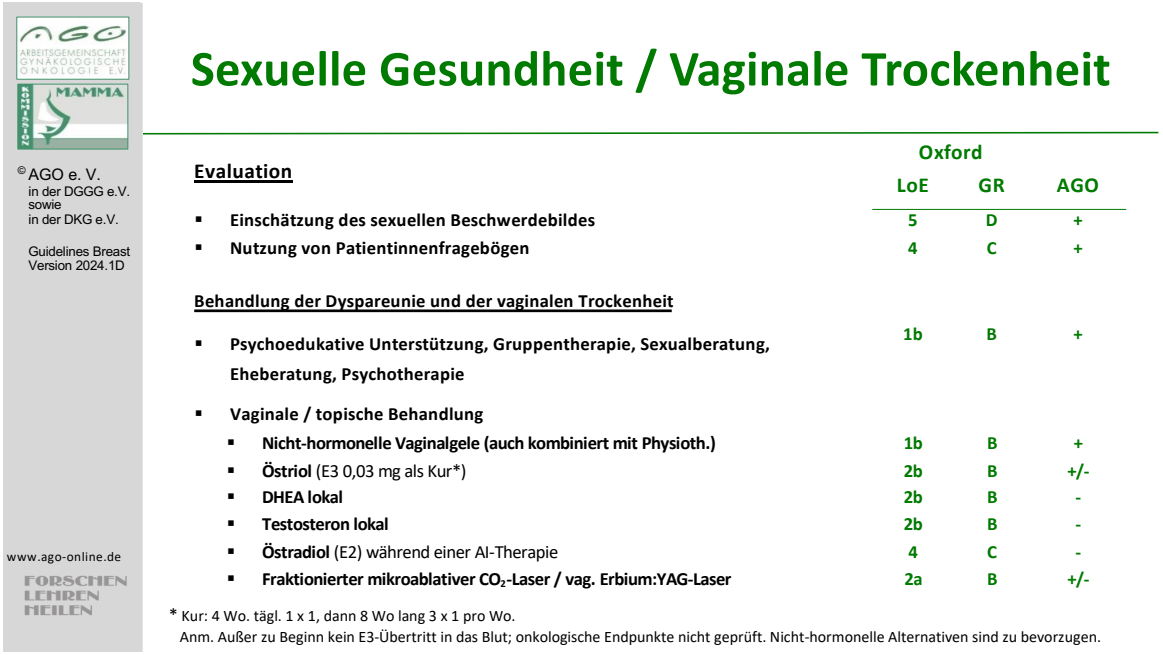
1. Moormann PG, Havrilesky LJ, Giersch JM et al. Oral contraceptives and risk of ovarian cancer and breast cancer among high-risk women: a systematic review and meta-analysis.J Clin Oncol. 2013 Nov 20;31(33):4188-98.
2. Lambertini M, Massarotti C, Havas et al. Contraceptive Use in Premenopausal Women With Early Breast Cancer. JAMA Netw Open. 2022;5(9)
3. Fitzpatrick D, Pirie K, Reeves G, et al. (2023) Combined and progestagen-only hormonal contraceptives and breast cancer risk: A UK nested case–control study and meta-analysis. PLoS Med 20(3): e1004188

LNG-IUDs

1. Dominick S et al: Levonogestrel intrauterine system for endometrial protection in women with breast cancer on adjuvant tamoxifen. Cochrane Database syst Rev 2015; Dec 9; 12: CD007245.
2. Soini T, Hurskainen R, Grénman S et al.: Levonorgestrel-releasing intrauterine system and the risk of breast cancer: A nationwide cohort study. Acta Oncol. 2016 Feb;55(2):188-92.
3. Yun Fu Zhigang Zhuang: Long-term effects of levonorgestrel-releasing intrauterine system on tamoxifen-treated breast cancer patients: a meta-analysis Int J Clin Exp Pathol 2014; 7 (10) 6419-6429
4. Fu Y, Zhuang Z. Long-term effects of levonorgestrel-releasing intrauterine system on tamoxifen-treated breast cancer patients: a meta-analysis. Int J Clin Exp Pathol. 2014 Sep 15;7(10):6419-29. eCollection 2014. Review.

Emergency Contraception - Options after Diagnosis of Breast Cancer

1. Casay PM et al: Caring for breast cancer survivor‘s health and well being WJCO 2014;10: 5 (4): 693-704



Reviews:

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

Sexual Complaints Screener For Women:

1. Burri A, Porst H. Preliminary Validation of a German Version of the Sexual Complaints Screener for Women in a Female Population Sample. Sex Med. 2018 Jun;6(2):123-130.
2. 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.
3. Isidori AM, Pozza C, Esposito K et al. Development and validation of a 6-item version of the female sexual function index (FSFI) as a diagnostic tool for female sexual dysfunction. J Sex Med. 2010 Mar;7(3):1139-46.

Treatment of vaginal dryness:

Education, Group therapy, counselation:

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.
2. Huynh V, Vemuru S, Hampanda K, et al. No One-Size-Fits-All: Sexual Health Education Preferences in Patients with Breast Cancer. Ann Surg Oncol. 2022;29(10):6238-6251.

Non-hormonal treatment:

1. Juraskova I, Jarvis S, Mok K et al. The acceptability, feasibility, and efficacy (phase I/II study) of the OVERcome (Olive Oil, Vaginal Exercise, and MoisturizeR) intervention to improve dyspareunia and alleviate sexual problems in women with breast cancer. J Sex Med. 2013 Oct;10(10):2549-58.

Vaginal topic treatment

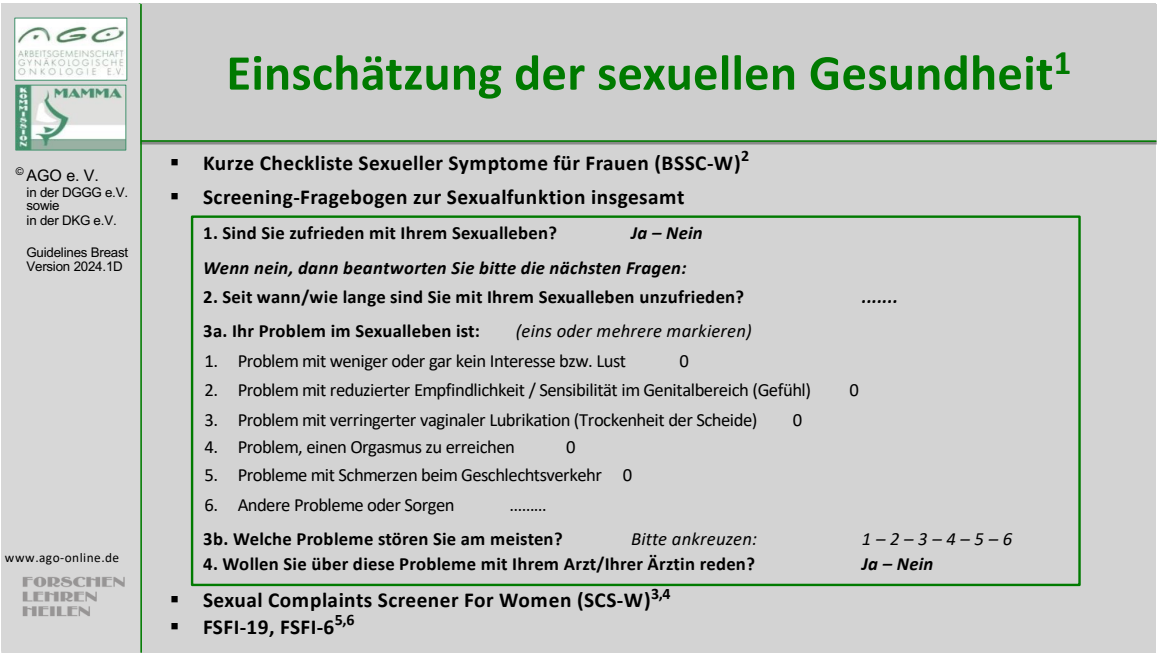
1. Donders G, Belle G, Neven P et al.: Effect of ultra-low-dose estriol and lactobacilli vaginal tablets (Gynoflor®) on inflammatory and infectious markers of the vaginal ecosystem in postmenopausal women with breast cancer on aromatase inhibitors. Eur J Clin Microbiol Infect Dis (2015) 34:2023–2028
2. 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)
3. 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.
4. 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
5. Kim YH, Park S, Lee M et al.: Effect of a pH-Balanced Vaginal Gel on Dyspareunia and Sexual Function in Breast Cancer Survivors Who Were Premenopausal at Diagnosis: A Randomized Controlled Trial. Obstet Gynecol. 2017;129(5):870-6.
6. 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.
7. Barton DL, Sloan JA, Shuster LT et al. Evaluating the efficacy of vaginal dehydroepiandosterone for vaginal symptoms in postmenopausal cancer survivors: NCCTG N10C1 (Alliance). Support Care Cancer. 2018 Feb;26(2):643-650. doi: 10.1007/s00520-017-3878-2.
8. 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.
9. Labrie F, Archer DF, Koltun W et al. Efficacy of intravaginal dehydroepiandrosterone (DHEA) on moderate to severe dyspareunia and vaginal dryness, symptoms of vulvovaginal atrophy, and of the genitourinary syndrome of menopause. Menopause. 2018 Nov;25(11):1339-1353.
10. Mitchell CM, Reed SD, Diem S et al. Efficacy of Vaginal Estradiol or Vaginal Moisturizer vs Placebo for Treating Postmenopausal Vulvovaginal Symptoms: A Randomized Clinical Trial. JAMA Intern Med. 2018 May 1;178(5):681-690.
11. Chatsiproios D, Schmidts-Winkler IM, König L et al. Topical treatment of vaginal dryness with a non-hormonal cream in women undergoing breast cancer treatment - An open prospective multicenter study. PLoS One. 2019 Jan 24;14(1):e0210967.
12. 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.
13. 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.
14. The North American Menopause Society (NAMS). The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society. Menopause. 2020;27(9):976-992.
15. Lubián López DM. Management of genitourinary syndrome of menopause in breast cancer survivors: An update. World J Clin Oncol. 2022 Feb 24;13(2):71-100. doi: 10.5306/wjco.v13.i2.71. PMID: 35316932; PMCID: PMC8894268.

Laser therapy

1. Areas F, Valadares ALR, Conde DM, Costa-Paiva L: The effect of vaginal erbium laser treatment on sexual function and vaginal health in women with a history of breast cancer and symptoms of the genitourinary syndrome of menopause: a prospective study. Menopause 2019, 26:1052-8.
2. Athanasiou S, Pitsouni E, Douskos A et al.: Intravaginal energy-based devices and sexual health of female cancer survivors: a systematic review and meta-analysis. Lasers Med Sci 2019.
3. Cruz VL, Steiner ML, Pompei LM et al.: Randomized, double-blind, placebo-controlled clinical trial for evaluating the efficacy of fractional CO2 laser compared with topical estriol in the treatment of vaginal atrophy in postmenopausal women. Menopause. 2018 Jan;25(1):21-28. doi: 10.1097/GME.0000000000000955.
4. Gambacciani M, Levancini M, Russo E et al. Long-term effects of vaginal erbium laser in the treatment of genitourinary syndrome of menopause. Climacteric. 2018 Apr;21(2):148-152. doi: 10.1080/13697137.2018.1436538. Epub 2018 Feb 13.

5. Jha S, Wyld L, Krishnaswamy PH: The Impact of Vaginal Laser Treatment for Genitourinary Syndrome of Menopause in Breast Cancer Survivors: A Systematic Review and Meta-analysis. Clin Breast Cancer 2019, 19:e556-e62.
6. Pearson A, Booker A, Tio M, Marx G: Vaginal CO2 laser for the treatment of vulvovaginal atrophy in women with breast cancer: LAAVA pilot study. Breast Cancer Res Treat 2019, 178:135-40.
7. Quick AM, Zvinovski F, Hudson C et al.: Fractional CO2 laser therapy for genitourinary syndrome of menopause for breast cancer survivors. Support Care Cancer 2019.
8. Salvatore S, Pitsouni E, Del Deo F et al.: Sexual Function in Women Suffering From Genitourinary Syndrome of Menopause Treated With Fractionated CO2 Laser. Sex Med Rev. 2017;5(4):486-94.
9. Sussman TA, Kruse ML, Thacker HL, et al. Managing Genitourinary Syndrome of Menopause in Breast Cancer Survivors Receiving Endocrine Therapy. Journal of oncology practice / American Society of Clinical Oncology 2019, 15:363-70
10. Siliquini GP, Bounous VE, Novara L, et al. Fractional CO_2 vaginal laser for the genitourinary syndrome of menopause in breast cancer survivors. Breast J. 2021 May;27(5):448-455.



General recommendations

1. 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

Brief Sexual Symptom Checklist (BSSC-W)

1. Bijlsma-Rutte A, Braamse AMJ, van Oppen P et al. Screening for sexual dissatisfaction among people with type 2 diabetes in primary care. J Diabetes Complications. 2017 Nov;31(11):1614-1619.

Sexual Complaints Screener For Women (SCS-W) (Langversion und Kurzversion):

1. Giraldi A, Rellini A, Pfaus JG et a.. Questionnaires for assessment of female sexual dysfunction: a review and proposal for a standardized screener. J Sex Med. 2011 Oct;8(10):2681-706.
2. Burri A, Porst H. Preliminary Validation of a German Version of the Sexual Complaints Screener for Women in a Female Population Sample. Sex Med. 2018 Jun;6(2):123-130.

Female Sexual Function Index (FSFI-19, FSFI-6):

1. 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.
2. Isidori AM, Pozza C, Esposito K, et al. Development and validation of a 6-item version of the female sexual function index (FSFI) as a diagnostic tool for female sexual dysfunction. J Sex Med. 2010 Mar;7(3):1139-46.