



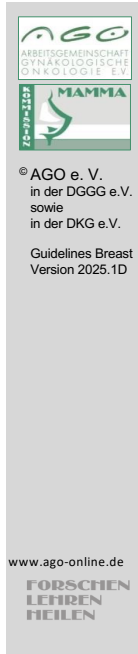
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Guidelines Breast  
Version 2025.1D

FORSCHEN  
LEHREN  
HEILEN

# Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

## Gynäkologische Probleme, Schwangerschaft und Reproduktion bei Mammakarzinompatientinnen



## Gynäkologische Probleme, Schwangerschaft und Reproduktion bei Mammakarzinompatientinnen

- **Versionen 2015–2024:**  
Albert / Bauerfeind / Blohmer / Fehm / Fersis / Gerber / Hanf /  
Hooper/ Loibl / Maas / Mundhenke /Reimer / Rody / Scharl /  
Stickeler/ Thill / Thomssen / Witzel
- **Version 2025:**  
Park-Simon / Witzel

### Screened data bases:

Pubmed	2009 –2024
ASCO	2009 - 2024
SABCS	2009 - 2024

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

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

\* Schema: 4 Wo. tägl. 1 x 1, dann 8 Wo lang 3 x 1 pro Wo., dann Fortführung 1-2 x pro Woche - 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. 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.
5. 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.
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7. 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. van Barele M, Heemskerk-Gerritsen BAM, Louwers YV, et al. Estrogens and Progestogens in Triple Negative Breast Cancer: Do They Harm? *Cancers (Basel)*. 2021 May 21;13(11):2506. doi: 10.3390/cancers13112506. PMID: 34063736; PMCID: PMC8196589.
2. 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. 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.
2. 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.
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### Ospemifeme

1. 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.
2. 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.
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### Topical Vaginal Application:

1. 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.
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  3. 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.
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  6. 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
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  9. 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.
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## Weitere Methoden zur Erleichterung postmenopausaler Symptome nach Mamma-Ca I

### Medikamentöse Ansätze\* (Reduktion von Hitzewallungen):

- **Selektive Serotonin-Reuptake-Inhibitoren und Serotonin-(Noradrenalin) Reuptake-Inhibitoren (SSRI-SNRI):**
  - Venlafaxin
  - Desvenlafaxin, Sertralin, Citalopram
- **Gabapentin** (MaCa-Pat. unter Tamoxifen-Therapie)
- **Neurokinin-3 Rezeptor Antagonisten (Fezolinetant)** (cave: onkologische Sicherheit nicht untersucht)
- **Pregabalin**
- **Clonidin** 0,05-0,15 mg/die (MaCa-Pat. unter Tamoxifen-Therapie)
- **Oxybutynin** (2,5 mg / 5 mg)
- **MPA** (i.m. 500 mg single shot, wirksam, aber endokrin aktiv)
- **Vitamin E**

### Medikamentöse Ansätze (andere Therapieziele):

- **Melatonin** (verbesserte Schlafqualität)
- **Duloxetin** (zur Therapie von Arthralgien nur unter AI-Therapie)
- **Omega 3 Fettsäuren** (zur Therapie von Arthralgien nur unter AI-Therapie)

\* Beachte: Substantieller Placebo-Effekt nachgewiesen (23-57%) LoE 1b A +

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

- Gallagher S, Johnstone A, De Livera A, et al. A survey of women diagnosed with breast cancer experiencing oncology treatment-induced hot flushes: identification of specific characteristics as predictors of hot flush occurrence, frequency, and severity. *J Cancer Surviv.* 2024 Jul 31. doi: 10.1007/s11764-024-01647-7. Epub ahead of print. PMID: 39085555.
- Kingsberg S, Banks V, Caetano C, et al. Treatment utilization and non-drug interventions for vasomotor symptoms in breast cancer survivors taking endocrine therapy: Real-world findings from the United States and Europe. *Maturitas.* 2024 Oct;188:108071. doi: 10.1016/j.maturitas.2024.108071. Epub 2024 Jul 23. PMID: 39059108.

### Venlafaxine

- 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.
- 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.
- 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.
- Taleghani SY, Etesam F, Esfandbod M. Evaluation and Comparison of Citalopram and Venlafaxine for Management of Hot Flashes in Women with Breast Cancer. *Drug Res (Stuttg).* 2023 Oct;73(8):465-472. doi: 10.1055/a-2061-7020. Epub 2023 Aug 30. PMID: 37647930.

### Desvenlafaxine

1. Kim Y, Yeom CW, Lee HJ, et al. Differential effects of desvenlafaxine on hot flashes in women with breast cancer taking tamoxifen: a randomized controlled trial. NPJ Breast Cancer. 2024 Jul 17;10(1):59. doi: 10.1038/s41523-024-00668-w. PMID: 39019875; PMCID: PMC11255222.

### 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. Taleghani SY, Etesam F, Esfandbod M. Evaluation and Comparison of Citalopram and Venlafaxine for Management of Hot Flashes in Women with Breast Cancer. Drug Res (Stuttg). 2023 Oct;73(8):465-472. doi: 10.1055/a-2061-7020. Epub 2023 Aug 30. PMID: 37647930.

### Gabapentin

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### Neurokinin-3. Rezeptor Antagonisten:

1. Fraser GL, Lederman S, Waldbaum A, et al. A phase 2b, randomized, placebo-controlled, double-blind, dose-ranging study of the neurokinin 3 receptor antagonist fezolinetant for vasomotor symptoms associated with menopause. *Menopause*. 2020;27(4):382-392.
2. Depypere H, Timmerman D, Donders G, et al. Treatment of Menopausal Vasomotor Symptoms With Fezolinetant, a Neurokinin 3 Receptor Antagonist: A Phase 2a Trial. *J Clin Endocr Metab*. 2019;104(12):5893-5905.
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### Pregabalin

1. 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. doi: 10.1016/j.ajog.2019.12.011. Epub 2019 Dec 20. PMID: 31870736.

### 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

### 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.

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

1. 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. 2020 May;28(5):2139-2143. doi: 10.1007/s00520-019-05013-7. Epub 2019 Aug 11. PMID: 31402403.
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3. Prior JC, Nielsen JD, Hitchcock CL et al.: Medroxyprogesterone and conjugated oestrogen are equivalent for hot flashes: a 1-year randomized double-blind trial following premenopausal ovariectomy. Clin Sci (Lond). 2007;112(10):517–525.

#### Vitamine E

1. Rada G: Non-hormonal interventions for hot flashes 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 flashes in breast cancer survivors: gabapentin vs. vitamin E. Climacteric. 2009 Aug;12(4):310-8.

#### **Sleep disturbances**

##### 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

#### **Aromatase-inhibitor induced arthralgia**

1. Bae K, Lamoury G, Carroll S, et al. Comparison of the clinical effectiveness of treatments for aromatase inhibitor-induced arthralgia in breast cancer patients: A systematic review with network meta-analysis. Crit Rev Oncol Hematol. 2023 Jan;181:103898. doi: 10.1016/j.critrevonc.2022.103898. Epub 2022 Dec 16. PMID: 36535489.

##### Duloxetine

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#### Omega fatty acid

1. Hershman DL, Unger JM, Crew KD, et al. Randomized Multicenter Placebo-Controlled Trial of Omega-3 Fatty Acids for the Control of Aromatase Inhibitor-Induced Musculoskeletal Pain: SWOG S0927. *J Clin Oncol*. 2015 Jun 10;33(17):1910-7. doi: 10.1200/JCO.2014.59.5595. Epub 2015 May 4. PMID: 25940724; PMCID: PMC4451174
2. 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.

# CAM\*-Therapie

## Postmenopausale Symptome II

\* Complementary and Alternative Medicine

Bei laufender onkologischer Standardtherapie: CAVE: Medikamenten-Interaktionen!	Oxford		
	LoE	GR	AGO
▪ <b>Soja – Isoflavonoide*</b>			
Hitzewallungen	1b	B	-
Schlafstörungen	1b	B	-
Topische vaginale Applikation	1b	B	+/-
▪ <b>Rotklee – Isoflavonoide*</b>			
Hitzewallungen und Schlafstörungen	1b	B	+/-
▪ <b>Leinsamen (40 g/d)</b> (bei HR+ ≤ 10g/d (1Essl.)) (mögl. Reduktion des Rezidivrisikos, keine Reduktion v. Hitzewallungen)	2b	B	+/-
▪ <b>Traubensilberkerze gegen Hitzewallungen</b>	1b	B	+/-
Traubensilberkerze und Johanniskraut als fixe Kombi	1b	B	+/-
▪ <b>Johanniskraut-Produkte</b> (Cave: Pharmakokinetische Interferenz mit endokriner Therapie, Zytostatika und Tyrosinkinase-Inhibitoren)	1b	B	+/-
▪ <b>Ginseng Wurzel</b> (Panax ginseng or P. quinquefolius)	1b	B	-
▪ <b>Bromelain + Papain + Selen + Lektin (Al-induzierte Gelenksbeschwerden)</b>	3b	B	+
▪ <b>Homöopathische Mittel zur Reduktion Hitzewallungen</b> (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.
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### Soy- derived 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. 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.
3. 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.
4. 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.
5. 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.
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  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]
  9. Shakeri F: Effectiveness of red clover in alleviating of menopausal symptoms: A 12-week randomized, controlled trial. *Climacteric*. 2015;18(4):568-73.

#### 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. Castelo-Branco C, Gambacciani M, Cano A, et al. Review & meta-analysis: isopropanolic black cohosh extract iCR for menopausal symptoms - an update on the evidence. *Climacteric*. 2021 Apr;24(2):109-119. doi: 10.1080/13697137.2020.1820477. Epub 2020 Oct 6. PMID: 33021111.
2. Fritz H, Seely D, McGowan J, et al. Black cohosh and breast cancer: a systematic review. *Integr Cancer Ther*. 2014;13:12-29
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4. Kim MS: Ginseng for managing menopause symptoms: a systematic review of randomized clinical trials. *J Ginseng Res*. 2013 Mar;37(1):30-6.
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- on menopausal hot flashes. *J Educ Health Promot*. 2018 Mar 1;7:36. doi: 10.4103/jehp.jehp\_81\_17. eCollection 2018.
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#### Sodium selenite, proteolytic plant enzymes (bromelaine and papain), and Lens culinaris lectin

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#### 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	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* (Elektro-) Akupunktur	5	D	+
▪ Aromatase-Inhibitor induzierte Arthralgie	1a	B	+
▪ Hitzewallungen	2a	B	+
▪ Angst, Depressionen	2b	B	+
▪ Schlafstörungen	2a	C	+

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#### Cognitive behavioral therapy, Hypnosis

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## Sexuelle Gesundheit / Vaginale Trockenheit

<u>Evaluation</u>	Oxford		
	LoE	GR	AGO
▪ Einschätzung des sexuellen Beschwerdebildes	5	D	+
▪ Nutzung von Patientinnenfragebögen	4	C	+
<u>Behandlung der Dyspareunie und der vaginalen Trockenheit</u>			
▪ Psychoedukative Unterstützung, Gruppentherapie, Sexualberatung, Eheberatung, Psychotherapie	1b	B	+
▪ Vaginale / topische Behandlung			
▪ Nicht-hormonelle Vaginalgele (auch kombiniert mit Physioth.)	1b	B	+
▪ Östriol (E3 0,03 mg*)	2b	B	+/-
▪ DHEA lokal	2b	B	-
▪ Testosteron lokal	2b	B	-
▪ Östradiol (E2) während einer AI-Therapie	4	C	-
▪ Fraktionierter mikroablativer CO <sub>2</sub> -Laser / vag. Erbium:YAG-Laser	1b	B	+/-

\* Schema: 4 Wo. tägl. 1 x 1, dann 8 Wo lang 3 x 1 pro Wo., dann Fortführung mit 1-2 x pro Woche  
Anm. Außer zu Beginn kein E3-Übertritt in das Blut; onkologische Endpunkte nicht geprüft. Nicht-hormonelle Alternativen sind zu bevorzugen.

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### Evaluation

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#### Education, Group therapy, counselation:

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#### 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

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### 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.
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## Ovarschutz und Fertilitätserhalt bei prämenopausalen Patientinnen

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li>CTx + GnRHa (zur Prophylaxe des ovariellen Funktionsausfalls, GnRHa-Applikation &gt; 2 Wochen vor Chemotherapie, unabhängig vom Hormonrezeptorstatus)</li> </ul>	1a	A	+
<ul style="list-style-type: none"> <li>CTx + GnRHa (zur Erhöhung der Schwangerschaftsrate)</li> </ul>	2a	B	+/-
<ul style="list-style-type: none"> <li>Angebot zur Beratung über Fertilitätserhalt inkl. assistierter Reproduktion (ART) (Information: <a href="https://fertiprotekt.com">https://fertiprotekt.com</a>; S2k-Leitlinie Fertilitätserhalt bei onkologischen Erkrankungen)</li> </ul>			++
<ul style="list-style-type: none"> <li> <ul style="list-style-type: none"> <li>Kryokonservierung Oozyten (unbefruchtet / befruchtet) nach ovarieller Stimulation<sup>1</sup></li> </ul> </li> </ul>	2a	C	+
<ul style="list-style-type: none"> <li> <ul style="list-style-type: none"> <li>Kryokonservierung Ovargewebe mit anschließender Transplantation<sup>2</sup></li> </ul> </li> </ul>	4	D	+
<ul style="list-style-type: none"> <li>Assistierte Reproduktion nach Mammakarzinom<sup>1</sup></li> </ul>	4	C	+/-

<sup>1</sup> Evidenzlage z.T. eingeschränkt auf Grund der Studienlage (keine prospektiv randomisierten Studien möglich)

<sup>2</sup> Risiko durch Tumorzellverschleppung bei Transplantation des Gewebes; bei Mutationsträgerinnen komplette Explantation des Transplantats nach Schwangerschaft notwendig

### Ovarian function protection

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.
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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

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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

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#### 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.
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#### Cryoconservation of oocytes after ovarian stimulation:

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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.
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## Ovarian Protection – Synopsis of Randomized Trials

	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. 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.



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## Oncological Safety of controlled ovarian stimulation (COS) or assisted reproductive therapy (ART)

N = 15 studies including 4643 patients undergoing COS or ART (assisted reproductive therapy)

**COS before starting treatment (n=11 studies):**  
 Reduced risk of recurrence RR 0.58, 95% CI 0,46-0,73  
 Reduced risk of mortality RR 0.54, 95% CI 0,38-0,76  
 No detrimental effect on EFS 0,76, 95% CI 0,55-1,06  
 - Subgroup of HR positive pts. HR 0.36, 95% CI 0.20–0.65

**ART after treatment (n=4 studies):**  
 Reduced risk of recurrence (RR 0.34, 95% CI 0.17-0.70)  
 No detrimental effect EFS (HR 0.43, 95% CI 0.17-1.11).

**Conclusion: COS at diagnosis or ART following breast cancer treatment completion does not appear to be associated with any detrimental prognostic effect in young women**

*Arecco et al. Human Reprod 2022*

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.

## Einschätzung der ovariellen Reserve

	Oxford		
	LoE	GR	AGO
<b>Tests zur Beurteilung der ovariellen Reserve</b>			
▪ Anti-Müller Hormon	1b	B	+
▪ Antrale Follikelzählung	3b	B	+
▪ FSH	2b <sup>a</sup>	B	+
▪ Kombinierte Testverfahren zur Einschätzung der ovariellen Reserve*	5	C	+
<b>Geringere ovarielle Reserve bei BRCAmt</b>	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, 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, Niu J, 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.

## Brustkrebs in Schwangerschaft und Stillzeit\*

### – Diagnostik und OP –

	Oxford		
	LoE	GR	AGO
▪ <b>Mammadiagnostik wie außerhalb der Schwangerschaft (keine grundsätzliche MRT-Indikation)</b>	4	C	++
▪ <b>Staging: wenn indiziert (Knochenszintigraphie nach Entbindung)</b>	5	D	+
▪ <b>Ganzkörper MRT ohne Kontrastmittel</b>	4	C	+/-
▪ <b>OP wie bei Nicht-Schwangeren</b>	4	C	++
▪ <b>Sentinel-Node Biopsie (nur Technetium)</b>	2a	B	+
▪ SLNE im 1. Trimester	5	D	+/-
▪ Sensitivität und Spezifität sind unklar (während Stillzeit); Stillen sollte für 24 Stunden vermieden werden	4	C	++
▪ Farbstoffblau ( <u>keine Studiendaten in der Schwangerschaft</u> )	4	C	--

\* Teilnahme an Registerstudie empfohlen

Study link: <http://germanbreastgroup.de/studien/adjuvant/brustkrebs-in-der-schwangerschaft.html>

1. Loibl S, Azim HA Jr, Bachelot T et al. ESMO Expert Consensus Statements on the management of breast cancer during pregnancy (PrBC). Ann Oncol. 2023 Oct;34(10):849-866.
2. Peccatori FA 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. Loibl S, Schmidt A, Gentilini O, et al. Breast Cancer Diagnosed During Pregnancy: Adapting Recent Advances in Breast Cancer Care for Pregnant Patients. JAMA Oncol. 2015 Nov;1(8):1145-53.

Outcome information (e.g. GBG registry)

1. Amant F, von Minckwitz G, Han SN, et al. Prognosis of women with primary breast cancer diagnosed during pregnancy: results from an international collaborative study. J Clin Oncol. 2013 Jul 10;31(20):2532-9.
2. Loibl S, Han SN, von Minckwitz G, et al. Treatment of breast cancer during pregnancy: an observational study. Lancet Oncol. 2012 Sep;13(9):887-96.
3. Raphael J, Trudeau ME, Chan K. Outcome of patients with pregnancy during or after breast cancer: a review of the recent literature. Curr Oncol. 2015 Mar;22(Suppl 1):S8-S18

Statement: Breast imaging & biopsy like in non-pregnant

1. Athanasiou A, Appelman L, Pijnappel RM, et al. ESR Essentials: diagnostic work-up in patients with symptomatic breast disease- practice recommendations by the European Society of Breast Imaging. Eur Radiol. 2024 Jul 31. doi: 10.1007/s00330-024-10980-5.
2. Di Florio-Alexander RM, Slanetz PJ, Moy L et al. ACR Appropriateness Criteria((R)) Breast Imaging of Pregnant and Lactating Women. Journal of the American College of Radiology : JACR 2018;15(11s):S263-s75.
3. Peccatori FA et al. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24 Suppl 6:vi160-70
4. Zafrakas M, Papasozomenou P, Gereade A, et al. Screening and Diagnostic Mammography During Pregnancy and Lactation: A Systematic Review of the Literature. Cureus. 2024 Aug 8;16(8):e66465. doi: 10.7759/cureus.66465.

Statement: Staging: ultrasound, chest X-ray if indicated

1. Wang PI, et al. Imaging of pregnant and lactating patients: part 2, evidence-based review and recommendations. AJR Am J Roentgenol 2012;198:785-792.

Statement: Whole Body MRI

1. Han SN, Amant F, Michielsen K, et al. Feasibility of whole-body diffusion-weighted MRI for detection of primary tumor, nodal and distant metastases in women with cancer during pregnancy: a pilot study. Eur Radiol. 2017 Dec 7.
2. Peccatori FA, Codacci-Pisanelli G, Del Grande M, et al. Whole body MRI for systemic staging of breast cancer in pregnant women. Breast. 2017 Oct;35:177-181.

Statement: Surgery like in non-pregnant patients

1. Annane K et al. Infiltrative breast cancer during pregnancy and conservative surgery. Fetal Diagn Ther 2005, 20: 442-444
2. Kuerer H et al., Conservative surgery and chemotherapy for breast carcinoma during pregnancy. Surgery 2002, 131: 108-110
3. Berry DL et al., Management of breast cancer during pregnancy using a standardized protocol J Clin Oncol 1999, 17: 855-861
4. Genin AS, De Rycke Y, Stevens D, et al. Association with pregnancy increases the risk of local recurrence but does not impact overall survival in breast cancer: A case-control study of 87 cases. Breast. 2015 Oct 8. pii: S0960-9776(15)00207-6.

Statement: „Sentinel node biopsy“ during pregnancy

1. Bothou A, Margioulas-Siarkou C, Petousis S, et al. Sentinel lymph node biopsy for breast cancer during pregnancy: A comprehensive

- update. Eur J Clin Invest. 2024 Mar;54(3):e14134
2. Han SN, Amant F, Cardonick EH, et al. Axillary staging for breast cancer during pregnancy: feasibility and safety of sentinel lymph node biopsy. Breast Cancer Res Treat 2018;168(2):551-57.
  3. Gropper AB, Calvillo KZ, Dominici L, et al. Sentinel lymph node biopsy in pregnant women with breast cancer. Ann Surg Oncol. 2014 Aug;21(8):2506-11.

### Reviews

1. Loibl S, von Minckwitz G, et al., Breast carcinoma during pregnancy. Cancer. 2006 Jan 15;106(2):237-46.
2. Shachar SS, Gallagher K, McGuire K, et al. Multidisciplinary Management of Breast Cancer During Pregnancy. Oncologist 2017;22(3):324-34.
3. Lee GE, Mayer EL, Partridge A. Prognosis of pregnancy-associated breast cancer. Breast Cancer Res Treat 2017;163(3):417-21.
4. Ruiz R, Herrero C, Strasser-Weippl K, et al. Epidemiology and pathophysiology of pregnancy-associated breast cancer: A review. Breast 2017;35:136-41.
5. Talele AC, Slanetz PJ, Edmister WB, et al. The lactating breast: MRI findings and literature review. Breast J 2003, 9: 237-240
6. Hachar SS, Gallagher K, McGuire K et al. Multidisciplinary Management of Breast Cancer During Pregnancy. Oncologist 2017;22(3):324-34.
7. Framarino-Dei-Malatesta M, Sammartino P, Napoli A. Does anthracycline-based chemotherapy in pregnant women with cancer offer safe cardiac and neurodevelopmental outcomes for the developing fetus? BMC Cancer 2017;17(1):777.
8. Ben Brahim E, Mrad K, Driss M, et al. Placental metastasis of breast cancer. Gynecol Obstet Fertil 2001, 29: 545-548
9. Gelber S et al. Effect of pregnancy on overall survival after diagnosis of early stage breast cancer. JCO 2001; 19: 1671-5
10. Peccatori FA et al. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24 Suppl 6:vi160-70

## Brustkrebs in Schwangerschaft und Stillzeit – (Neo-)adjuvante Therapie –

	Oxford		
	LoE	GR	AGO
▪ <b>Bestrahlung während der Schwangerschaft</b>	<b>4</b>	<b>C</b>	<b>-</b>
▪ <b>(Neo-)adjuvante Chemotherapie ab dem zweiten Trimenon (Indikation wie bei Nicht-Schwangeren)</b>			<b>++</b>
▪ Antrazykline: AC, EC	<b>2b</b>	<b>B</b>	<b>++</b>
▪ Dosisdichte Regime mit Einsatz von kurz-wirksamen GCSF	<b>4</b>	<b>C</b>	<b>+/-</b>
▪ Taxane	<b>2a</b>	<b>B</b>	<b>++</b>
▪ Platinsalze (Carboplatin, Cisplatin)	<b>4</b>	<b>C</b>	<b>+/-</b>
▪ MTX (z. B. CMF)	<b>4</b>	<b>D</b>	<b>--</b>
▪ <b>Endokrine Therapie</b>	<b>4</b>	<b>D</b>	<b>--</b>
▪ <b>Anti-HER2-Therapie</b>	<b>3a</b>	<b>C</b>	<b>--</b>
▪ <b>Checkpointinhibitoren</b>	<b>4</b>	<b>D</b>	<b>--</b>
▪ <b>Bisphosphonate, Denosumab</b>	<b>4</b>	<b>D</b>	<b>--</b>

Die Behandlung (Systemtherapie, Operation, RT) des Mammakarzinoms in der Schwangerschaft soll so nah wie möglich an der Standardbehandlung junger, nicht-schwangerer Patientinnen mit Mammakarzinom ausgerichtet sein.

### General principles

1. Amant F, Nekljudova V, Maggen C, et al: Outcome of breast cancer patients treated with chemotherapy during pregnancy compared with non-pregnant controls. Eur J Cancer 2022;170:54–63.
2. Loibl S, Azim HA Jr., Bachelot T, et al. ESMO Expert Consensus on the management of breast cancer during pregnancy (PrBC). Ann Oncol 2023; 34(10): 849-866.

### Statement: Radiotherapy during pregnancy

1. Kal HB et al., Radiotherapy during pregnancy: fact and fiction. Lancet Oncol 2005, 6: 328-333 (Review)

### Statement: (Neo-)adjuvant chemotherapy only after first trimester (indication as in non-pregnant)

1. Auger N, Maniraho A, Ayoub A, Arbour L. Association of maternal cancer with congenital anomalies in offspring. Paediatr Perinat Epidemiol. 2023 Dec 19.
2. Ring et al, Chemotherapy for breast cancer during pregnancy: An 18-Year experience from five London teaching Hospitals. J Clin Oncol 2005, 23: 4192-4197
3. Mir O et al. Emerging therapeutic options for breast cancer chemotherapy during pregnancy. Ann Oncol. 2008 Apr;19(4):607-13.
4. Del Gobbo A, et al. Chemotherapy for breast cancer during pregnancy induces vascular alterations and impaired development of

placental villi: A preliminary histopathological study. Eur J Obstet Gynecol Reprod Biol. 2020;250:155–161 (11).

5. Vandembroucke T, et al. Child development at 6 years after maternal cancer diagnosis and treatment during pregnancy. International Network on Cancer, Infertility and Pregnancy (INCIP). Eur J Cancer 2020;138:57–67

#### Statement: Anthracyclines: AC, EC

1. Amant F et al. Long-term cognitive and cardiac outcomes after prenatal exposure to chemotherapy in children aged 18 months or older: an observational study. Lancet Oncol 2012;13:256-264.
2. Cardonick E, Gilmandyar D, Somer RA. Maternal and neonatal outcomes of dose-dense chemotherapy for breast cancer in pregnancy. Obstet Gynecol. 2012 Dec;120(6):1267-72.
3. Loibl S, Han SN, Amant F. Being Pregnant and Diagnosed with Breast Cancer. Breast Care (Basel). 2012 Jun;7(3):204-209. Epub 2012 Jun 27.
4. Loibl S et al. Treatment of breast cancer during pregnancy: an observational study. Lancet Oncol. 2012 13(9):887-96.
5. Peccatori FA, Azim HA Jr, Scarfone G, et al. Weekly epirubicin in the treatment of gestational breast cancer (GBC). Breast Cancer Res Treat. 2009 Jun;115(3):591-4.

#### Omission of 5FU based on the same evidence as in non-pregnant patients (GIM2 study) - see also chapter on adjuvant chemotherapy

1. Del Mastro L, De Placido S, Bruzzi P et al. Gruppo Italiano Mammella (GIM) investigators. Fluorouracil and dose-dense chemotherapy in adjuvant treatment of patients with early stage breast cancer: an open-label, 2x2 factorial, randomised phase 3 trial. Lancet. 2015 May 9;385(9980):1863-72.

#### Statement: Taxanes

1. Aranda-Gutierrez A, Ferrigno Guarjardo AS, Vaca-Cartagena BF, et al. Obstetric and neonatal outcomes following taxane use during pregnancy: a systematic review. BMC Cancer 2024; 24 (1): 9.
2. Ferrigno Guajardo AS, Vaca-Cartagena BF, et al. Taxanes for the treatment of breast cancer during pregnancy: an international cohort study. J Natl Cancer Inst. 2024 Feb 8;116(2):239-248.

#### Statement: Platinum salts

1. Calsteren KV, Verbesselt R, Devlieger R, et al. Transplacental transfer of paclitaxel, docetaxel, carboplatin, and trastuzumab in a baboon model. Int J Gynecol Cancer 2010 Dec;20(9):1456-64.

2. Köhler C, Oppelt P, Favero G, et al. How much platinum passes through the placental barriers? Analysis of platinum applications in 21 patients with cervical cancer during pregnancy. *Am J Obstet Gynecol.* 2015 Aug;213(2):206.
3. Kong TW, Lee EJ, Lee Y, et al. Neoadjuvant and postoperative chemotherapy with paclitaxel plus cisplatin for the treatment of FIGO stage IB cervical cancer in pregnancy. *Obstet Gynecol Sci.* 2014 Nov;57(6):539-43.
4. Zheng X, Zhu Y, Zhao Y, et al. Taxanes in combination with platinum derivatives for the treatment of ovarian cancer during pregnancy: A literature review. *International journal of clinical pharmacology and therapeutics* 2017;55(9):753-60.

Statement: MTX (e.g. CMF)

1. Ring et al., Chemotherapy for breast cancer during pregnancy: An 18-Year experience from five London teaching Hospitals. *J Clin Oncol* 2005, 23: 4192-4197

Statement: Endocrine treatment

1. Cunha GR, Taguchi O, Namikawa R, et al. Teratogenic effects of clomiphene, tamoxifen, and diethylstilbestrol on the developing human female genital tract *Hum Pathol.* 1987;18:1132–1143.
2. Isaacs RJ, Hunter W, Clark K. Tamoxifen as systemic treatment of advanced breast cancer during pregnancy — case report and literature review. *Gynecol Oncol.* 2001;80:405-408.

Statement Trastuzumab during pregnancy

1. Andrikopoulou A, Apostolidou K, Chatzinikolaou S, et al.: an update. *BMC Cancer* 2021;21:463.
2. Azim HA Jr et al. Pregnancy occurring during or following adjuvant trastuzumab in patients enrolled in the HERA trial (BIG 01-01). *Breast Cancer Res Treat.* 2012;133(1):387-91.
3. Lambertini M, Martel S, Campbell C et al. Pregnancies during and after trastuzumab and/or lapatinib in patients with human epidermal growth factor receptor 2-positive early breast cancer: Analysis from the NeoALTTO (BIG 1-06) and ALTTO (BIG 2-06) trials. *Cancer* 2018.
4. Paluch-Shimon S, Cardoso F, Partridge AH, et al.: ESO-ESMO fifth international consensus guidelines for breast cancer in young women (BCY5). *Ann Oncol* 2022;33:1097–1118.
5. Yildirim N, Bahceci A. Use of pertuzumab and trastuzumab during pregnancy. *Anticancer Drugs* 2018;29(8):810-13.
6. Sarno MA et al. Are monoclonal antibodies a safe treatment for cancer during pregnancy? *Immunotherapy* 2013; 5(7):733-41.
7. Zagouri F et al. Trastuzumab administration during pregnancy: a systematic review and meta-analysis. *Breast Cancer Res Treat.* 2013

Jan;137(2):349-57.

Statement Immunotherapy during pregnancy

1. Garutti M, Lambertini M, Puglisi F: Checkpoint inhibitors, fertility, pregnancy, and sexual life: a systematic review. ESMO Open 2021;6:100276.
2. Borgers JSW, et al. Immunotherapy for cancer treatment during pregnancy. Lancet Oncol. 2021 Dec;22(12):e550-e561. doi: 10.1016/S1470-2045(21)00525-8..

Statement Bisphosphonate during pregnancy

1. Levy S, Fayez I, Taguchi N et al. Pregnancy outcome following in utero exposure to bisphosphonates. Bone. 2009 Mar;44(3):428-30.
2. Amant F, Loibl S, Neven P, et al. Breast cancer in pregnancy. Lancet. 2012 Feb 11;379(9815):570-9. Review.

General information: Chemotherapy during pregnancy

1. Murthy RK, Theriault RL, Barnett CM, et al. Outcomes of children exposed in utero to chemotherapy for breast cancer. Breast Cancer Res. 2014 Dec 30;16(6):3414.

## Brustkrebs in Schwangerschaft und Stillzeit\* – Entbindung und Stillen –

	Oxford		
	LoE	GR	AGO
▪ Entbindung erst bei ausreichender kindlicher Reife	2b	C	++
▪ Eine Beendigung der Schwangerschaft verbessert den mütterlichen Erkrankungsverlauf nicht	3b	C	
▪ Entbindungsmodus wie bei gesunden Schwangeren; Entbindung im Leukozytennadir nach Chemotherapie sollte vermieden werden	4	C	++
▪ Sollte eine Systemtherapie nach der Entbindung fortgeführt werden, kann Stillen evtl. kontraindiziert sein (cave: Toxizität !)	5	D	++

\* Teilnahme an Registerstudie empfohlen

### General principles

1. Paluch-Shimon S, Cardoso F, Partridge AH, et al.: ESO-ESMO fifth international consensus guidelines for breast cancer in young women (BCY5). Ann Oncol 2022;33:1097–1118.
2. Loibl S, Azim HA Jr., Bachelot T, et al. ESMO Expert Consensus on the management of breast cancer during pregnancy (PrBC). Ann Oncol 2023; 34(10): 849-866.

### Statements: Delivery should be postponed until sufficient fetal maturation since termination of pregnancy does not improve maternal outcome

1. Loibl S, Han SN, von Minckwitz G, et al. Treatment of breast cancer during pregnancy: an observational study. Lancet Oncol 2012;13:887-896.

### Statements: Delivery mode like in non-pregnant; Avoid delivery in leucocyte nadir

1. Berry DL et al., Management of breast cancer during pregnancy using a standardized protocol J Clin Oncol 1999, 17: 855-861

### Statements: If further systemic therapy is needed after delivery, breast feeding may be contraindicated depending on drug toxicities

1. Williams Obstetrics lecture book

2. Pistilli B et al. Chemotherapy, targeted agents, antiemetics and growth-factors in human milk: how should we counsel cancer patients about breastfeeding? *Cancer Treat Rev.* 2013;39(3):207-11.
3. Hays KE, Ryu RJ, Swisher EM et al. Duration of cisplatin excretion in breast milk. *Journal of human lactation : official journal of International Lactation Consultant Association* 2013;29(4):469-72.

## Brustkrebs in Schwangerschaft und Stillzeit\*

### – Prognose –

	<b>Oxford LoE</b>
<ul style="list-style-type: none"> <li>■ <b>Mammakarzinom während Schwangerschaft</b> <ul style="list-style-type: none"> <li>■ Prognose wird nicht verschlechtert, wenn korrekte Behandlung</li> </ul> </li> </ul>	<b>3a</b>
<ul style="list-style-type: none"> <li>■ <b>Mammakarzinom während der Stillzeit bzw. im ersten Jahr nach der Schwangerschaft</b> <ul style="list-style-type: none"> <li>■ Prognose schlechter als während der Schwangerschaft und ohne Bezug zur Schwangerschaft</li> </ul> </li> </ul>	<b>3a</b>
<ul style="list-style-type: none"> <li>■ <b>Schwangerschaft / Laktation nach Mammakarzinom</b> <ul style="list-style-type: none"> <li>■ Prognose wird nicht verschlechtert</li> </ul> </li> </ul>	<b>3a</b>

\* Teilnahme an Registerstudie empfohlen

#### General principles

1. Amant F, Lefrère H, Borges VF, et al.: The definition of pregnancy-associated breast cancer is outdated and should no longer be used. Lancet Oncol 2021;22:753–754.
2. Amant F, Nekljudova V, Maggen C, et al: Outcome of breast cancer patients treated with chemotherapy during pregnancy compared with non-pregnant controls. Eur J Cancer 2022;170:54–63.
3. Amant F, Loibl S, Neven P, et al. Breast cancer in pregnancy. Lancet. 2012 Feb 11;379(9815):570-9.
4. Loibl S, Han SN, von Minckwitz G, et al. Treatment of breast cancer during pregnancy: an observational study. Lancet Oncol 2012;13:887-896.
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## Brustkrebs in Schwangerschaft\* – Familienplanung –

	Oxford		
	LoE	GR	AGO
▪ <b>Mammakarzinompatientinnen im gebärfähigen Alter sollten eine Beratung über Fertilität und Fertilitäts-erhalt vor Therapiebeginn erhalten.</b>	5	D	++
▪ <b>Assistierte Reproduktion nach Mammakarzinom</b>	4	C	+/-
▪ <b>Die Erfolgsaussichten für eine intakte Schwangerschaft bzw. ein Kind sind bei autologer Eizellverwendung bei Mammakarzinom-patientinnen geringer als bei Nicht-Karzinompatientinnen.</b>	3b	D	
▪ <b>Von einer Schwangerschaft soll nach einer Mammakarzinom-erkrankung nicht abgeraten werden. Dies gilt grundsätzlich unabhängig vom Hormonrezeptorstatus und auch gBRCA Status.</b>	2a	B	
▪ <b>ET Unterbrechung (max. 2 Jahre nach mind. 18 Monate Vortherapie) bei Kinderwunsch ohne kurzfristigen Überlebensnachteil</b>	2b	B	+

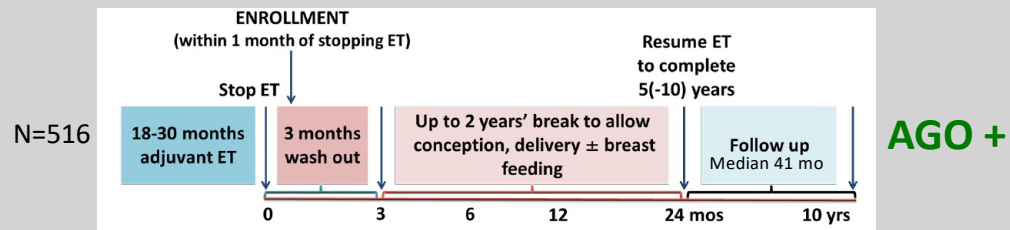
\* Teilnahme an Registerstudie empfohlen

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## Adjuvant endocrine therapy in premenopausal patients with pregnancy desire



Women under 42 years were studied:

- Outcome: 64% live births; 62% of mothers breastfed; 2% birth defects.
- A time-limited interruption of endocrine therapy to pursue pregnancy does not result in prognostic disadvantages (BCFI).
- Interruption of ET (maximum 2 years after at least 18 months of prior therapy) for pregnancy desire does not lead to short-term survival disadvantages.

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## Kontrazeptive Möglichkeiten für Brustkrebspatientinnen

	Oxford		
	LoE	GR	AGO
▪ <b>Barriere-Methoden</b>	5	D	+
▪ <b>Sterilisation (Tubenligatur / Salpingektomie / 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>Kombinierte orale Kontrazeptiva</b>	5	D	-
▪ <b>Optionen für Notfall-Kontrazeption</b>			
▪ Kupfer armierte Intrauterin-Devices (Cu-IUD)	5	D	+
▪ Levonorgestrel, Ulipristalacetat oral	5	D	+

### Contraception (general)

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### LNG-IUDs

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