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Guidelines Breast
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FORSCHEN
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Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Brustkrebs: Spezielle Situationen

Screened data bases: Pubmed 2007 - 2018, ASCO 2010 – 2018, SABCS 2010 – 2018, Cochrane Data Base (2017)

1. ABC Consensus Guidelines for Advanced Breast Cancer (ABC 1-4): Cardoso F, Costa A, Senkus E et al. 3rd ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 3). Ann Oncol. 2017 Jan 1;28(1):16-33.
2. Harbeck N, Lüftner D, Marschner N et al. ABC4 Consensus: assessment by a German Group of Experts. Breast Care (Basel). 2018 Mar;13(1):48-58.
3. ASCO (American Association of Clinical Oncology, Practice Guidelines, 2016) <http://www.asco.org>
4. American Society of Clinical Oncology Clinical Practice Survivorship Guidelines, Endorsements and Adaptations: <https://www.asco.org/sites/new-www.asco.org/files/content-files/practice-and-guidelines/documents/Survivorship-Summary-of-Recs-Binder.pdf>
5. 2016 Updated American Society of Clinical Oncology/Oncology Nursing Society Chemotherapy Administration Safety Standards, Including Standards for Pediatric Oncology: <http://ascopubs.org/doi/pdfdirect/10.1200/JOP.2016.017905>
6. Hershman DL, Lacchetti C, Dworkin RH et al. American Society of Clinical Oncology. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014 Jun 20;32(18):1941-67.

7. CMA (Canadian Medical Association , 2016): <http://www.cmaj.ca>
8. NCCN (National Comprehensive Cancer Network , 2018): <http://www.nccn.org>
9. NCI (National Cancer Institute , 2017): <http://www.cancer.gov>
10. S3 Leitlinie Supportive Therapie: Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.1, 2017, AWMF Registernummer: 032/054OL, <http://leitlinienprogramm-onkologie.de/Supportive-Therapie.95.0.html> (Zugriff 29. Januar 2018)



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Brustkrebs: Spezielle Situationen

■ Versionen 2005–2018:

Dall / Fehm / Fersis / Friedrich / Gerber / Göhring /
Harbeck / Huober / Janni / Loibl / Lück / Lux / Maass /
Mundhenke / Oberhoff / Rody / Scharl / Schneeweiss /
Schütz / Sinn / Solomayer / Thomssen

■ Version 2019:

Stickeler / Müller

Update January 2018 – Harbeck / Rody

Update January 2017 – Schütz / Sinn

Update January 2016 – Thomssen / Harbeck

Update January 2015 – Solomayer / Harbeck

Update January 2014 – Fehm/Schneeweiss

Update January 2013 – Fersis/Friedrich

Update January 2012 – Lux/Lück

Update February 2011 – Janni/Huober

Update January 2010 – Mundhenke/Rody

Screened data bases:


Pubmed 2000 – Jan 2019, ASCO 2005 – 2018, SABCS 2005 – 2018, ECCO/ESMO (2005 – 2018), EBCC (2005 – 2017), Cochrane data

base (2012),

Screened for: Clinical Trials, Meta-Analyses, Practice Guidelines, Randomized Controlled Trial, Reviews

Screened guidelines

- NCCN: http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf



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Brustkrebs: Spezielle Situationen

- „Junge“ Patientin
- Brustkrebs in der Schwangerschaft und Stillzeit
- „Ältere“ Patientin
- Mammakarzinom des Mannes
- Inflammatorisches Mammakarzinom
- Okkultes Karzinom CUP („Cancer of Unknown Primary“)
- Morbus Paget
- Maligner und Borderline Phylloides-Tumor
- Angiosarkome
- Brust-Implantat assoziiertes großzellig-anaplastisches Lymphom (BIA-ALCL)
- Metaplastisches Karzinom

1. Dietz JR, Partridge AH, Gemignani ML, et al.: Cancer Management Updates: Young and Older, Pregnant, or Male. Ann Surg Oncol. 2015 Oct;22(10):3219-24.

Brustkrebs bei der jungen Patientin ≤ 40 Jahre			
	Oxford		
	LoE	GR	AGO
▪ Meist ungünstige Tumorbiologie mit schlechter Prognose	2a	B	
▪ Lokalthherapie altersunabhängig	2b	B	+
▪ Leitliniengerechte (neo-)adjuvante Systemtherapie (siehe Therapiekapitel)	1b	A	++
▪ GnRH zur ovariellen Protektion (siehe Kap. Gyn. Probleme)	1a	B	+
▪ Angebot zur genetischen Beratung und Fertilitätsberatung	2b	B	++
▪ Frühzeitige Beratung zur Verhütung	2b	B	++

1. Poggio F, Lambertini M, Bighin C et al. Management of young women with early breast cancer. ESMO open 2018;3(Suppl 1):e000458.
2. Paluch-Paluch-Shimon S, Pagani O, Partridge AH, et al. ESO-ESMO 3rd international consensus guidelines for breast cancer in young women (BCY3). Breast. 2017 Oct;35:203-217.
3. Ribnikar D, Ribeiro JM, Pinto D et al.: Breast cancer under age 40: a different approach. Curr Treat Options Oncol. 2015 Apr;16(4):16.
4. Pursche T, Hedderich M, Heinrichs A et al. Guideline conformity treatment in young women with early-onset breast cancer in Germany. Breast Care (Basel). 2014 Oct;9(5):349-54
5. Cardoso F, Loibl S, Pagani O, et al: European Society of Breast Cancer Specialists. The European Society of Breast Cancer Specialists recommendations for the management of young women with breast cancer. Eur J Cancer. 2012 Dec;48(18):3355-77

Prognosis in young women

1. Shoemaker ML, White MC, Wu M et al. Differences in breast cancer incidence among young women aged 20-49 years by stage and tumor characteristics, age, race, and ethnicity, 2004-2013. *Breast Cancer Res Treat* 2018;169(3):595-606.
2. Ann H. Partridge et al. Model Program to Improve Care for a Unique Cancer Population: Young Women With Breast Cancer *J Oncol Pract*. 2012; 8(5): e105–e110.
3. Hironaka-Mitsuhashi A, Tsuda H, Yoshida M et al. Invasive breast cancers in adolescent and young adult women show more aggressive immunohistochemical and clinical features than those in women aged 40-44 years. *Breast Cancer* 2018.
4. Johansson ALV, Trewin CB, Hjerkind KV et al. Breast cancer-specific survival by clinical subtype after 7 years follow-up of young and elderly women in a nationwide cohort. *Int J Cancer* 2018.
5. Liu Z, Sahli Z, Wang Y, Wolff AC et al. Young age at diagnosis is associated with worse prognosis in the Luminal A breast cancer subtype: a retrospective institutional cohort study. *Breast Cancer Res Treat* 2018;172(3):689-702.
6. Kroman N. et al, Factors influencing the effect of age on prognosis in breast cancer: population based study. *BMJ*. 2000 Feb 19;320(7233):474-8.
7. Gonzalez-Angulo AM et al., Women age < or = 35 years with primary breast carcinoma: Disease features at presentation. *Cancer* 2005;103: 2466-2472
8. Rapiti E, et al. Survival of young and older breast cancer patients in Geneva from 1990 to 2001. *Eur J Cancer* 2005;41(10):1446-52.
9. Oh JL, Bonnen M, Outlaw ED, et al . The impact of young age on locooregional recurrence after doxorubicin-based breast conservation therapy in patients 40 years old or younger: How young is "young"? *Int J Radiat Oncol Biol Phys* 2006;65:1345-52.

10. Anders CK, Hsu DS, Broadwater G, et al . Young age at diagnosis correlates with worse prognosis and defines a subset of breast cancers with shared patterns of gene expression. J Clin Oncol 2008;26:3324-30.
11. Freedman RA et al. Management of breast cancer in very young women. Breast. 2013;22 Suppl 2:S176-9. J Natl Compr Canc Netw. 2013;11(9):1060-9.
12. Tichy JR et al. Breast cancer in adolescents and young adults: a review with a focus on biology. J Natl Compr Canc Netw. 2013;11(9):1060-9.

Chemotherapy in young women

1. Passildas J, Collard O, Savoye AM et al. Impact of Chemotherapy-induced Menopause in Women of Childbearing Age With Non-metastatic Breast Cancer - Preliminary Results From the MENOCOR Study. Clin Breast Cancer 2018.
2. Oktay K, Harvey BE, Partridge AH et al. Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol 2018;36(19):1994-2001.
3. Aebi S. Special issues related to the adjuvant therapy in very young women. Breast 2005, 14: 594-599 (Review)
4. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;365: 1687–1717
5. M. De Laurentiis et al. Taxane-based combinations as adjuvant chemotherapy of early breast cancer: a meta-analysis of randomized trials. J Clin Oncol 2008;26 (1),44–53.
6. Huober J et al. Effect of neoadjuvant anthracycline-taxane-based chemotherapy in different biological breast cancer phenotypes: overall results from the GeparTrio study. Breast Cancer Res Treat. 2010;124:133–140.

7. Loibl S, Jackisch C, Lederer B et al. Outcome after neoadjuvant chemotherapy in young breast cancer patients: a pooled analysis of individual patient data from eight prospectively randomized controlled trials. *Breast Cancer Res Treat.* 2015 Jul;152(2):377-87.

Endocrine therapy in young women

1. Cuzick J, Ambroisine L, Davidson N, et al. LHRH-agonists in Early Breast Cancer Overview group Use of luteinising-hormone-releasing hormone agonists as adjuvant treatment in premenopausal patients with hormone-receptor-positive breast cancer: a meta-analysis of individual patient data from randomised adjuvant trials. *Lancet.* 2007;369(9574):1711-23.
2. C. Davies et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. *Lancet* 2013;381,805–816
3. Gray RG, et al. aTTom: Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years in 6,953 women with early breast cancer. *J Clin Oncol* 2013; 31(suppl): abstr 5
4. Love RR, Laudico AV, Van Dinh N et al. Timing of adjuvant surgical oophorectomy in the menstrual cycle and disease-free and overall survival in premenopausal women with operable breast cancer. *J Natl Cancer Inst.* 2015 Mar 19;107(6):djv064.

Benefit from trastuzumab

1. Smith I, HERA study team: 2-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomised controlled trial. *Lancet.* 2007;369(9555):29-36
2. A.H. Partridge et al. The effect of age on breast cancer outcomes in women with her-2 positive breast cancer: results from the

HERA trial J Clin Oncol 2013;44,2692–2698

Benefit from temporary amenorrhoea after adjuvant chemotherapy (chemotherapy induced or GnRHa-related)

1. M. Gnant et al. Endocrine therapy plus zoledronic acid in premenopausal breast cancer. N Engl J Med 2009;360 (7) 679–691
2. Gerber B et al. Effect of Luteinizing Hormone-Releasing Hormone Agonist on ovarian function after adjuvant breast cancer chemotherapy: by the GBG 37 ZORO study. J. Clin Oncol 2011;29 (17) 2334-2341
3. Adjuvant Breast Cancer Trials Collaborative Group. Ovarian ablation or suppression in premenopausal early breast cancer: results from the international adjuvant breast cancer ovarian ablation or suppression randomized trial J Natl Cancer Inst 2007 ;99:516–525
4. S.M. Swain, J.H. Jeong, C.E. Geyer Jr., et al. Longer therapy, iatrogenic amenorrhea, and survival in early breast cancer. N Engl J Med 2010 ; (362);2053–2065
5. Del Mastro L 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 2013 in press
6. Yang B et al. Concurrent treatment with gonadotropin-releasing hormone agonists for chemotherapy-induced ovarian damage in premenopausal women with breast cancer: a meta-analysis of randomized controlled trials Breast 2013;22(2):150-7.
7. Recchia F, Necozone S, Bratta M, et al. LH-RH analogues in the treatment of young women with early breast cancer: Long-term follow-up of a phase II study. Int J Oncol. 2015 Mar;46(3):1354-60.
8. Kim J, Kim M, Lee JH et al. Ovarian function preservation with GnRH agonist in young breast cancer patients: does it impede the

effect of adjuvant chemotherapy? Breast. 2014 Oct;23(5):670-5.

9. Moore HCF, Unger JM, Phillips KA, et al Phase III trial (Prevention of Early Menopause Study [POEMS]-SWOG S0230) of LHRH analog during chemotherapy (CT) to reduce ovarian failure in early-stage, hormone receptor-negative breast cancer: An international Intergroup trial of SWOG, IBCSG, ECOG, and CALGB (Alliance). J Clin Oncol 32:5s, 2014 (suppl; abstr LBA505)

Surgery in young women (Surgery like ≥ 35 y - in particular BCT)


1. de Bock GH et al., Isolated loco-regional recurrence of breast cancer is more common in young patients and following breast conserving therapy; Long-term results of European Organisation for Research and Treatment of Cancer Studies. Eur J Cancer 2005, 25.
2. Garg AK et al. Effect of postmastectomy radiotherapy in patients <35 years old with stage II-III breast cancer treated with doxorubicin-based neoadjuvant chemotherapy and mastectomy. Int J Radiat Oncol Biol Phys. 2007 Dec 1;69(5):1478-83. – Radiation boost therapy can reduce in-breast recurrence [Bartelink H, Horiot JC, Poortmans PM, Struikmans H, et al. Impact of radiation dose on local control, fibrosis and survival after breast conserving treatment: 10 year results of the EORTC trial 22881-10882. Br Cancer Res Treat 2006;100:S8-10].
3. Mahmood U et al. Similar survival with breast conservation therapy or mastectomy in the management of young women with early-stage breast cancer. Int J Radiat Oncol Biol Phys.2012;83(5):1387e93.
4. Cao JQ et al. Comparison of recurrence and survival rates after breast-conserving therapy and mastectomy in young women with breast cancer. Curr Oncol. 2013;20(6):e593-e601. Review.
5. Recio-Saucedo A, Gerty S, Foster C, et al. Information requirements of young women with breast cancer treated with mastectomy or breast conserving surgery: A systematic review. Breast. 2016 Feb;25:1-13.

6. Frandsen J, Ly D, Cannon G, et al. In the Modern Treatment Era, Is Breast Conservation Equivalent to Mastectomy in Women Younger Than 40 Years of Age? A Multi-Institution Study. *Int J Radiat Oncol Biol Phys*. 2015 Dec 1;93(5):1096-103.
7. Vila J, Gandini S, Gentilini O. Overall survival according to type of surgery in young (≤ 40 years) early breast cancer patients: A systematic meta-analysis comparing breast-conserving surgery versus mastectomy. *Breast*. 2015 Jun;24(3):175-81.

Genetic and fertility counselling

1. Copson ER, Maishman TC, Tapper WJ et al. Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study. *Lancet Oncol* 2018;19(2):169-80.
2. Engel C, Rhiem K, Hahnen E et al. Prevalence of pathogenic BRCA1/2 germline mutations among 802 women with unilateral triple-negative breast cancer without family cancer history. *BMC Cancer* 2018;18(1):265.
3. Yang B et al: Concurrent treatment with gonadotropin-releasing hormone agonists for chemotherapy-induced ovarian damage in premenopausal women with breast cancer: A meta-analysis of randomized controlled trials. *Breast* 2013 Jan 5. pii: S0960-9776(12)00252-4.
4. Gerber B. et al. Effect of Luteinizing Hormone-Releasing Hormone Agonist on ovarian function after adjuvant breast cancer chemotherapy: by the GBG 37 ZORO study. *J. Clin Oncol* 29 (17) 2334-2341 2011
5. Del Mastro L et al: Effect of the Gonadotropin-Releasing Hormone Analogue Triptorelin on the occurrence of chemotherapy-induced early menopause in premenopausal women with breast cancer *JAMA* 306 (3); 269-276 2011
6. Ruddy KJ et al. Menopausal symptoms and fertility concerns in premenopausal breast cancer survivors: A comparison to age- and gravidity-matched controls. *Menopause*. 2011;18:105–108

7. Lee MC et al.: Fertility and reproductive considerations in premenopausal patients with breast cancer. *Cancer Control*. 2010 Jul;17(3):162-72.
8. Partridge AH EP. Gelber S, Peppercorn J et al. Fertility and menopausal outcomes in young breast cancer survivors. *Clin Breast Cancer* 2008; (:65-69
9. Hulvat MC, Jeruss JS. Maintaining fertility in young women with breast cancer. *Curr Treat Options Oncol*. 2009 Dec;10(5-6):308-17.
10. Ruddy KJ, Gelber SI, Tamimi RM, et al. Prospective study of fertility concerns and preservation strategies in young women with breast cancer. *J Clin Oncol*. 2014 Apr 10;32(11):1151-6.
11. 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 Dec;26(12):2408-19.

<div>  Brustkrebs in der Schwangerschaft* – Diagnostik und OP – </div>			
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ■ Diagnostik wie außerhalb der Schwangerschaft (keine grundsätzliche MRT-Indikation) 	4	C	++
<ul style="list-style-type: none"> ■ Staging: wenn indiziert (Knochenszintigraphie nach Entbindung) 	5	D	+
<ul style="list-style-type: none"> ■ Ganzkörper MRT ohne Kontrastmittel 	4	C	+/-
<ul style="list-style-type: none"> ■ OP wie bei Nicht-Schwangeren 	4	C	++
<ul style="list-style-type: none"> ■ Sentinel-Node Biopsie (nur Technetium) 	4	C	+
<ul style="list-style-type: none"> ■ SNB im 1. Trimester <ul style="list-style-type: none"> ■ Sensitivität und Spezifität sind unklar (während Stillzeit); Stillen sollte für 24 Stunden vermieden werden 	5	D	+/-
<ul style="list-style-type: none"> <ul style="list-style-type: none"> ■ Farbstoffblau (keine Studiendaten in der Schwangerschaft) 	4	C	--
* Teilnahme an Registerstudie empfohlen			

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

1. 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
2. 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. diFlorio-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.
2. Bock K. et al., Rationale for a diagnostic chain in gestational breast tumor diagnosis. Arch Gynecol Obstet 2005
3. Ahn BY et al., Pregnancy and lactation-associated breast cancer: mammographic and sonographic findings. J Ultrasound Med 2003, 491-497
4. Nicklas AH et al., Imaging strategies in the pregnant cancer patient. Semin Oncol 2000, 27: 623-632
5. Hogge JP et al., Imaging and management of breast masses during pregnancy and lactation. Breast J 1999, 5: 272-283.
6. 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

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. Han SN, Amant F, Cardonick EH, Loibl S, Peccatori FA, Gheysens O, 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.
2. 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.
3. Khara SY, Kiluk JV, Hasson DM et al. Pregnancy-associated breast cancer patients can safely undergo lymphatic mapping. Breast J. 2008 May-Jun;14(3):250-4

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, Zagar TM, Faso A, Muss HB, 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, Touya D, St Louis J, Bukowski A, 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. Shachar 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. Scharl A, Ahr A, Göhring U-J: Malignome in der Schwangerschaft. In: Kaufmann M, Costa SD, Scharl A (eds) Die Gynäkologie. Springer, Heidelberg, 2002 pp 509
9. Gadducci A, Cosio S, Fanuchi A, et al; Chemotherapy with epirubicin and paclitaxel for breast cancer during pregnancy: case report and a review of the literature. Anticancer Res 2003; 23: 5225-5229
10. Ben Brahim E, Mrad K, Driss M, et al. Placental metastasis of breast cancer. Gynecol Obstet Fertil 2001, 29: 545-548
11. Gelber S et al. Effect of pregnancy on overall survival after diagnosis of early stage breast cancer. JCO 2001; 19: 1671-5
12. 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



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Brustkrebs in der Schwangerschaft – (Neo-)adjuvante Therapie –

Oxford		
LoE	GR	AGO
4	C	-
		++
2b	B	++
2b	B	+
4	C	+/-
4	D	--
4	D	--
3a	C	--
4	D	-

- **Bestrahlung während der Schwangerschaft**
- **(Neo-)adjuvante Chemotherapie ab dem zweiten Trimenon (Indikation wie bei Nicht-Schwangeren)**
 - Antrazykline: AC, EC
 - Taxane
 - Platinsalze (Carboplatin, Cisplatin)
 - MTX (e.g. CMF)
- **Endokrine Therapie**
- **Anti-HER2-Therapie**
- **Bisphosphonate, Denosumab**

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. 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
2. 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.

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. Loibl S, Han S, Mayer K, et al. Neoadjuvant chemotherapy for patients with breast cancer during pregnancy (BCP). J Clin Oncol 32:5s, 2014 (suppl; abstr 1071)
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.

Statement: Anthracyclines: AC, EC

1. Loibl S, von Minckwitz G, et al., Breast carcinoma during pregnancy. Cancer. 2006 Jan 15;106(2):237-46.
2. Peccatori F et al. Weekly epirubicin in the treatment of gestational breast cancer (GBC). Breast Cancer Res Treat 2008; Aug 20 [epub ahead of print]
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. 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.
5. Loibl S et al. Treatment of breast cancer during pregnancy: an observational study. Lancet Oncol. 2012 13(9):887-96.
6. 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.

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. Mir O et al. Emerging therapeutic options for breast cancer chemotherapy during pregnancy. Ann Oncol. 2008 Apr;19(4):607-13.
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Statement: Platinum salts

1. 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.
2. Zheng X, Zhu Y, Zhao Y, Feng S, Zheng C. 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.
3. 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.
4. 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.

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.
3. C. Davies et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. Lancet 2013;381,805–816.

Statement Trastuzumab during pregnancy


1. 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.
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5. Loibl S. New Therapeutic Options for Breast Cancer during Pregnancy. Breast Care 2008; 3:171-176. (table overview of trastuzumab cases)
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Statement Bisphosphonate during pregnancy

1. Levy S, Fayed I, Taguchi N et al. Pregnancy outcome following in utero exposure to bisphosphonates. Bone. 2009 Mar;44(3):428-30.
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General information: Chemotherapy during pregnancy

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Brustkrebs in der Schwangerschaft*

– Entbindung und Stillen –

Oxford		
LoE	GR	AGO
2b	C	++
3b	C	
4	C	++
5	D	++

- Entbindung erst bei ausreichender kindlicher Reife
- Eine Beendigung der Schwangerschaft verbessert den mütterlichen Erkrankungsverlauf nicht
- Entbindungsmodus wie bei gesunden Schwangeren; Entbindung im Leukozytennadir nach Chemotherapie sollte vermieden werden
- Sollte eine Systemtherapie nach der Entbindung fortgeführt werden müssen, kann Stillen evtl. kontraindiziert sein (cave: Toxizität !)

* Teilnahme an Registerstudie empfohlen

General principles

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

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 und Schwangerschaft*

– Familienplanung –

	Oxford		
	LoE	GR	AGO
▪ Nach einer Mammakarzinomkrankung kann mit Hilfe reproduktionsmedizinischer Verfahren eine Schwangerschaft angestrebt werden.	5	D	++
▪ Die Erfolgsaussichten für eine intakte Schwangerschaft bzw. ein Kind sind bei autologer Eizellverwendung bei Mammakarzinompatientinnen geringer als bei Nicht-Karzinompatientinnen.	5	D	++
▪ Mammakarzinompatientinnen im gebärfähigen Alter sollten eine Beratung über Fertilität und Fertilitätsersatz vor Therapiebeginn erhalten.	5	D	++
▪ Von einer Schwangerschaft soll nach einer Mammakarzinomkrankung nicht abgeraten werden. Dies gilt grundsätzlich unabhängig vom Hormonrezeptorstatus.	5	D	++

* Teilnahme an Registerstudie empfohlen



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Brustkrebs während Schwangerschaft*

– Prognose –

**Oxford
LoE**

■	Mammakarzinom während Schwangerschaft / Stillzeit	
■	Prognose wird nicht verschlechtert, wenn korrekte Behandlung	3a
■	Schwangerschaft / Laktation nach Mammakarzinom	
■	Prognose wird nicht verschlechtert	3a

* Teilnahme an Registerstudie empfohlen

General principles

1. Amant F, Loibl S, Neven P, et al. Breast cancer in pregnancy. Lancet. 2012 Feb 11;379(9815):570-9.
2. Loibl S, Han SN, von Minckwitz G, et al. Treatment of breast cancer during pregnancy: an observational study. Lancet Oncol 2012;13:887-896.
3. Peccatori FA, Lambertini M, Scarfone G et al. Biology, staging, and treatment of breast cancer during pregnancy: reassessing the evidences. Cancer biology & medicine 2018;15(1):6-13.
4. 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.
5. 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.

Statement: Breast cancer during pregnancy / lactation: Outcome not compromised, if treated adequately

1. Gerstl B, Sullivan E, Ives A et al. Pregnancy Outcomes After a Breast Cancer Diagnosis: A Systematic Review and Meta-analysis. Clin

Breast Cancer 2018;18(1):e79-e88.

2. Lambertini M, Kroman N, Ameye L et al. Long-term Safety of Pregnancy Following Breast Cancer According to Estrogen Receptor Status. *J Natl Cancer Inst* 2018;110(4):426-29.
3. Peccatori FA, Lambertini M, Scarfone G et al. Biology, staging, and treatment of breast cancer during pregnancy: reassessing the evidences. *Cancer biology & medicine* 2018;15(1):6-13.
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5. Peccatori FA, Lambertini M, Scarfone G et al. Biology, staging, and treatment of breast cancer during pregnancy: reassessing the evidences. *Cancer biology & medicine* 2018;15(1):6-13.
6. de Haan J, Verheecke M, Van Calsteren K et al. Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients. *Lancet Oncol* 2018;19(3):337-46.
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9. Rodriguez et al. Evidence of poorer survival in pregnancy-associated breast cancer. *Obstet Gynecol*. 2008 Jul;112(1):71-8
10. Stensheim H, Møller B, van Dijk T et al. Cause-specific survival for women diagnosed with cancer during pregnancy or lactation: a registry-based cohort study. *J Clin Oncol* 2009;27:45-51. doi:10.1200/JCO.2008.17.4110.
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12. Azim HA Jr., Santoro L, Russell-Edu W, et al. Prognosis of pregnancy-associated breast cancer: a meta-analysis of 30 studies. *Cancer Treat Rev* 2012;38:834-842.
13. Amant F et al. Prognosis of women with primary breast cancer diagnosed during pregnancy: results from an international collaborative study *J Clin Oncol*. 2013;31(20):2532-9.
14. Litton JK et al. Case control study of women treated with chemotherapy for breast cancer during pregnancy as compared with nonpregnant patients with breast cancer. *Oncologist*. 2013;18(4):369-76.


Statement: Pregnancy and lactation after breast cancer: Outcome not compromised

1. Gelber S et al. Effect of pregnancy on overall survival after diagnosis of early stage breast cancer. JCO 2001; 19: 1671-5: IBCSG-participants - matched pair analysis: 94 patients pregnant after treatment (RR 0.44 – 0.96; p=0.04).
2. Kroman N et al. Pregnancy after treatment of breast cancer--a population-based study on behalf of Danish Breast Cancer Cooperative Group. Acta Oncol. 2008;47(4):545-9
3. Azim HA Jr et al. Prognostic impact of pregnancy after breast cancer according to estrogen receptor status: a multicenter retrospective study. J Clin Oncol 2013;31:73-79.

Review articles

1. Del Mastro et al, Infertility and pregnancy after breast cancer: current knowledge and future perspectives. Cancer Treat Rev. 2006 Oct;32(6):417-22. Epub 2006 Jul 13. Review.
Kroman N, et al. Prognostic influence of pregnancy before, around, and after diagnosis of breast cancer. Breast. 2003 Dec;12(6):516-21.
2. Kroman N, et al. Should women be advised against pregnancy after breast-cancer treatment? Lancet. 1997 Aug 2;350(9074):319-22.
3. Azim HA Jr, Santoro L, Pavlidis N, Gelber S, Kroman N, Azim H, Peccatori FA. Safety of pregnancy following breast cancer diagnosis: a meta-analysis of 14 studies. Eur J Cancer. 2011 Jan;47(1):74-83. Epub 2010 Oct 11. Review.
4. Pagani O, Azim H Jr. Pregnancy after Breast Cancer: Myths and Facts. Breast Care (Basel). 2012 Jun;7(3):210-214. Epub 2012 Jun 27.
5. Valachis A, Tsali L, Pesce LL, et al. Safety of pregnancy after primary breast carcinoma in young women: a meta-analysis to overcome bias of healthy mother effect studies. Obstet Gynecol Surv. 2010 Dec;65(12):786-93.
6. Azim HA Jr, Santoro L, Russell-Edu W, et al. Prognosis of pregnancy-associated breast cancer: a meta-analysis of 30 studies. Cancer Treat Rev. 2012 Nov;38(7):834-42. Epub 2012 Jul 9. Review.
7. Amant F, Loibl S, Neven P, et al. Breast cancer in pregnancy. Lancet. 2012 Feb 11;379(9815):570-9.
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Oncol. 2013;24 Suppl 6:vi160-70



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Geriatrische Einschätzung

- Spezifische Algorithmen nicht existent
- Toleranz gegenüber onkologischen Behandlungen variiert erheblich („funktionelle Reserve“)
- Zur umfassenden geriatrischen Einschätzung (CGA) gehört die multidisziplinäre Auswertung der Prädiktoren für Morbidität und Mortalität älterer Menschen
 - Physische, mentale und psychosoziale Gesundheit
 - Basisaktivitäten des täglichen Lebens (Ankleiden, Körperpflege, Zubereiten des täglichen Essens, Medikamenteneinnahme, etc.)
 - Lebensumstände, soziales Netz, Verfügbarkeit von Hilfsdienstleistern
- Einschätzungsinstrumente:
 - Charlson Comorbidity Index (breit eingesetzt; verlässliche Prädiktion über 10 Jahre)
 - 12 Prognosefaktoren zur Abschätzung des 4-Jahre-Sterberisikos
 - Kurze Screening-Tests (eher zur qualitativen Bewertung geeignet)
 - IADL (IADL = The Lawton Instrumental Activities of Daily Living Scale), G-8 Screening tool

1. Biganzoli L, Wildiers H, Oakman C et al. Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA). Lancet Oncol 2012;13(4):e148-60.
2. Overcash J. Comprehensive Geriatric Assessment: Interprofessional Team Recommendations for Older Adult Women With Breast Cancer. Clinical journal of oncology nursing 2018;22(3):304-15.
3. Charlson et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis 1987 40:373-383.
4. Lee et al. Development and validation of a prognostic index for 4-year mortality in older adults. JAMA 2006 295:801-08.
5. Wildes TM et al. Geriatric assessment is associated with completion of chemotherapy, toxicity, and survival in older adults with cancer. J Geriatr Oncol. 2013;4(3):227-34.
6. Aaldriks AA. Prognostic value of geriatric assessment in older patients with advanced breast cancer receiving chemotherapy et al. Breast 2013;22(5):753-60.
7. Bellera CA et al. Screening older cancer patients: first evaluation of the G-8 geriatric screening tool. Ann Oncol. 2012;23(8):2166-72

8. Aaldriks AA, Maartense E, Nortier HJ, et al. Prognostic factors for the feasibility of chemotherapy and the Geriatric Prognostic Index (GPI) as risk profile for mortality before chemotherapy in the elderly. *Acta Oncol.* 2016 Jan;55(1):15-23.



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Behandlung der „rüstigen älteren“ Patientin

(Lebenserwartung > 5 Jahre und akzeptable Komorbidität)

	Oxford		
	LoE	GR	AGO
▪ Bestimmung des aktuellen Gesundheitszustandes	2b	B	++
▪ Leitliniengerechte Behandlung	2a	C	++
▪ Operation wie bei „jüngeren“ Patientinnen	2b	B	++
▪ Hormontherapie (endokrin-sensibles Ca)	1a	A	++
▪ Chemotherapie (Standard Regime)			
▪ < 70 Jahre	1a	A	+
▪ > 70 Jahre	2a	C	+*
▪ Radiotherapie	1a	A	+
▪ Verzicht auf Radiotherapie in low risk, wenn eine endokrine Therapie geplant ist	1b	B	+
▪ Trastuzumab	2b	C	+

* Studienteilnahme wird empfohlen

1. Dietz JR, Partridge AH, Gemignani ML, et al. Breast Cancer Management Updates: Young and Older, Pregnant, or Male. Ann Surg Oncol. 2015 Oct;22(10):3219-24.

Statement: Treatment according to standard

1. Shachar SS, Jolly TA, Jones E et al. Management of Triple-Negative Breast Cancer in Older Patients: How Is It Different? Oncology (Williston Park) 2018;32(2):58-63.
2. Bouchardy C et al., Undertreatment strongly decreases prognosis of breast cancer in elderly women. J Clin Oncol. 2003;21(19):3580-71.
3. Quinten C, Kenis C, Hamaker M et al. The effect of adjuvant chemotherapy on symptom burden and quality of life over time; a preliminary prospective observational study using individual data of patients aged ≥ 70 with early stage invasive breast cancer. Journal of geriatric oncology 2018;9(2):152-62.
4. Schuil H, Derks M, Liefers GJ et al. Treatment strategies and survival outcomes in older women with breast cancer: A comparative study between the FOCUS cohort and Nottingham cohort. Journal of geriatric oncology 2018;9(6):635-41.
5. Ward SE, Richards PD, Morgan JL, Holmes GR, Broggio JW, Collins K, et al. Omission of surgery in older women with early breast

cancer has an adverse impact on breast cancer-specific survival. Br J Surg 2018;105(11):1454-63.

6. Enger SM: Breast cancer treatment of older women in integrated health care settings. J Clin Oncol. 2006 Sep 20;24(27):4377-83
7. Mustacchi G, Breast cancer in elderly women: a different reality? Results from the NORA study. Ann Oncol. 2007 Jun;18(6):991-6.
8. Chagpar AB: Determinants of early distant metastatic disease in elderly patients with breast cancer. Am J Surg. 2006 Sep;192(3):317-21
9. Kemeny MM: Barriers to clinical trial participation by older women with breast cancer. J Clin Oncol. 2003 Jun 15;21(12):2268-75
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12. Wildiers H: Management of breast cancer in elderly individuals: recommendations of the International Society of Geriatric Oncology. Lancet Oncol. 2007 Dec;8(12):1101-15
13. Luque M et al. Breast cancer management in the elderly. Clin Transl Oncol. 2013 epub

Statement: Surgery similar to „younger“ age

1. Swaminathan V. et al. Choices in Surgery for older women with breast cancer Breast Care 2012;7:445-451
2. Fentiman IS: Treatment of operable breast cancer in the elderly: a randomised clinical trial EORTC 10851 comparing tamoxifen alone with modified radical mastectomy. Eur J Cancer. 2003 Feb;39(3):309-16
3. Fentiman IS: Treatment of operable breast cancer in the elderly: a randomised clinical trial EORTC 10850 comparing modified radical mastectomy with tumorectomy plus tamoxifen. Eur J Cancer. 2003 Feb;39(3):300-8
4. Hind D: Surgery, with or without tamoxifen, vs tamoxifen alone for older women with operable breast cancer: cochrane review. Br J Cancer 2007 Apr 10;96(7):1025-9.
5. Rudenstam CM Randomized trial comparing axillary clearance versus no axillary clearance in older patients with breast cancer: first results of International Breast Cancer Study Group Trial 10-93. J Clin Oncol. 2006 Jan 20;24(3):337-44.
6. Martelli G, Miceli R, Daidone MG, et al. Axillary dissection versus no axillary dissection in elderly patients with breast cancer and no palpable axillary nodes: results after 15 years of follow-up. Ann Surg Oncol. 2011;18(1):125-33

7. Johnston SJ et al. A randomised trial of primary tamoxifen versus mastectomy plus adjuvant tamoxifen in fit elderly women with invasive breast carcinoma of high oestrogen receptor content: long-term results at 20 years of follow-up. *Ann Oncol* 2012;9:2296-300.
8. Chakrabarti J et al. A randomised trial of mastectomy only versus tamoxifen for treating elderly patients with operable primary breast cancer-final results at 20-year follow-up. *Crit Rev Oncol Hematol*. 2011;78(3):260-4.

Statement: Endocrine treatment (endocrine resp.)

1. Rugo HS, Turner NC, Finn RS et al. Palbociclib plus endocrine therapy in older women with HR+/HER2- advanced breast cancer: a pooled analysis of randomised PALOMA clinical studies. *Eur J Cancer* 2018;101:123-33.
2. Crivellari D, Sun Z, Coates AS, et al. Letrozole compared with tamoxifen for elderly patients with endocrine-responsive early breast cancer: The BIG 1-98 Trial. *J Clin Oncol* 2008; 26:1972-79
3. Muss H et al. Efficacy, toxicity, and quality of life in older women with early-stage breast cancer treated with letrozole or placebo after 5 years of tamoxifen: NCIC CTG intergroup trial MA.17. *J Clin Oncol*. 2008 Apr 20;26(12):1956-64
4. Lash TL: Physicians' assessments of adjuvant tamoxifen's effectiveness in older patients with primary breast cancer. *J Am Geriatr Soc*. 2005 Nov;53(11):1889-96
5. Silliman RA: Adjuvant tamoxifen prescription in women 65 years and older with primary breast cancer. *J Clin Oncol*. 2002 Jun 1;20(11):2680-8
6. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005;365(9472):1687-717
7. C. Davies et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. *Lancet* 2013;381, 805–816

Statement: Chemotherapy in pts. < 70 years

1. Loibl S, von Minckwitz G, Harbeck N, et al. Clinical feasibility of (neo)adjuvant taxane-based chemotherapy in older patients: analysis of >4,500 patients from four German randomized breast cancer trials. *Breast Cancer Res*. 2008 Sep16;10(5):R77

2. Fisher B: Treatment of axillary lymph node-negative, estrogen receptor-negative breast cancer: updated findings from National Surgical Adjuvant Breast and Bowel Project clinical trials. *J Natl Cancer Inst.* 2004 Dec 15;96(24):1823-31.
3. Fargeot P: Disease-free survival advantage of weekly epirubicin plus tamoxifen versus tamoxifen alone as adjuvant treatment of operable, node-positive, elderly breast cancer patients: 6-year follow-up results of the French adjuvant study group 08 trial. *J Clin Oncol.* 2004 Dec 1;22(23):4622-30
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5. De Maio E et al., Compliance and toxicity of adjuvant CMF in elderly breast cancer patients: a single-center experience. *BMC Cancer* 2005 24: 30
Muss HB et al., Adjuvant chemotherapy in older and younger women with lymph node-positive breast cancer. *JAMA* 2005, 293:1073-81.
6. Chagpar AB: Determinants of early distant metastatic disease in elderly patients with breast cancer. *Am J Surg.* 2006 Sep;192(3):317-21.
7. Hurria A et al., Patterns of toxicity in older patients with breast cancer receiving adjuvant chemotherapy. *Breast Cancer Res Treat.* 2005 92:151-6.
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Statement: Chemotherapy in pts. > 70 years

1. Qin A, Thompson CL, Silverman P. Predictors of late-onset heart failure in breast cancer patients treated with doxorubicin. *J Cancer Surviv.* 2015 Jun;9(2):252-9.
2. Pinder MC, Duan Z, Goodwin JS, et al. Congestive heart failure in older women treated with adjuvant anthracycline chemotherapy for breast cancer. *J Clin Oncol.* 2007 Sep 1;25(25):3808-15.
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4. Loibl S. et al Present Status of Adjuvant Chemotherapy for Elderly Breast Cancer Patients Breast Care 2012;7:439-444
5. Muss HB, Adjuvant chemotherapy in older women with early-stage breast cancer.N Engl J Med. 2009 May 14;360(20):2055-65.
6. Muss HB: CLGB: Toxicity of older and younger patients treated with adjuvant chemotherapy for node-positive breast cancer: the Cancer and Leukemia Group B Experience.J Clin Oncol. 2007 Aug 20;25(24):3699-704
7. Muss HB: Adjuvant treatment of elderly breast cancer patients. Breast. 2007 Nov;16 Suppl 2:159-65
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9. Crivellari D et al. Adjuvant pegylated liposomal doxorubicin for older women with endocrine nonresponsive breast cancer who are NOT suitable for a "standard chemotherapy regimen": the CASA randomized trial. Breast. 2013;22(2):130-7.

Statement: Radiotherapy

1. Kunkler I Radiotherapy issues in elderly breast cancer patients Breast Cancer Patients Breast Care 2012;7:453-459
2. Sautter M.L et al When are breast cancer patients old enough for the quitclaim of local control Strahlenther Onkol 2012 :1-5
3. Giordano SH Radiotherapy in older women with low-risk breast cancer: why did practice not change? 2012 J Clin Oncol 30 (14): 1577-1578
4. Prescott RJ: A randomised controlled trial of postoperative radiotherapy following breast-conserving surgery in a minimum-risk older population. The PRIME trial. Health Technol Assess. 2007 Aug;11(31):1-149, iii-iv
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Statement: Trastuzumab

1. Freedman RA, Vaz-Luis I, Barry WT, et al. Patterns of chemotherapy, toxicity, and short-term outcomes for older women receiving adjuvant trastuzumab-based therapy. *Breast Cancer Res Treat.* 2014 Jun;145(2):491-501.
2. Chavez-MacGregor M, Zhang N, Buchholz TA, et al. Trastuzumab-related cardiotoxicity among older patients with breast cancer. *J Clin Oncol.* 2013 Nov 20;31(33):4222-8
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4. Tan-Chiu E: Assessment of cardiac dysfunction in a randomized trial comparing doxorubicin and cyclophosphamide followed by paclitaxel, with or without trastuzumab as adjuvant therapy in node-positive, human epidermal growth factor receptor 2-overexpressing breast cancer: NSABP B-31. *J Clin Oncol.* 2005 Nov 1;23(31):7811-9
5. Smith I, HERA study team: 2-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomised controlled trial. *Lancet.* 2007 Jan 6;369(9555):29-36
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8. Brollo J et al. Adjuvant trastuzumab in elderly with HER-2 positive breast cancer: a systematic review of randomized controlled trials. *Cancer Treat Rev.* 2013;39(1):44-50

	Oxford		
	LoE	GR	AGO
▪ Reduzierte Standardtherapie	2b	C	++
▪ Therapieoptionen abgeleitet aus Studien mit älteren Patientinnen:			
▪ Keine Brustoperation (endokrine Therapieoption erwägen)	2b	C	+
▪ Keine Axilla-Op. (≥ 60 Jahre, cN0, Rez. pos.)	2b	B	+
▪ Keine Radiatio (≥ 65 Jahre, pT1, pN0, Rez. pos.)	1b	B	++
▪ Hypofraktionierte Radiatio	2b	B	+
▪ Keine Chemotherapie ≥ 70 Jahre bei negativer Risiko-Nutzen-Abwägung	2b	C	+

tamoxifen alone with modified radical mastectomy. Eur J Cancer (2003) 39(3):309-16

3. Fentiman IS, et al: Treatment of operable breast cancer in the elderly: a randomised clinical trial EORTC 10850 comparing modified radical mastectomy with tumorectomy plus tamoxifen. Eur J Cancer. 2003 Feb;39(3):300-8
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5. Balakrishnan A et al. Early operable breast cancer in elderly women treated with an aromatase inhibitor letrozole as sole therapy. Br J Cancer. 2011;105(12):1825-9.
6. Hamaker ME et al. Omission of surgery in elderly patients with early stage breast cancer. Eur J Cancer 2013;49(3):545-52.
7. Wink CJ et al. Hormone treatment without surgery for patients aged 75 years or older with operable breast cancer. Ann Surg Oncol. 2012;19(4):1185-91.

Statement: No axillary clearing (≥ 60 y, cN0, ER+)

1. Rudenstam CM, Randomized trial comparing axillary clearance versus no axillary clearance in older patients with breast cancer: first results of International Breast Cancer Study Group Trial 10-93. J Clin Oncol. 2006 Jan 20;24(3):337-44.
2. Martelli G: A randomized trial comparing axillary dissection to no axillary dissection in older patients with T1N0 breast cancer: results after 5 years of follow-up. Ann Surg. 2005 Jul;242(1):1-6
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Statement: No radiotherapy (≥ 70 y, pT1, pN0, ER+)

1. Kim YJ, Shin KH, Kim K. Omitting Adjuvant Radiotherapy for Hormone ReceptorPositive Early-Stage Breast Cancer in Old Age: A Propensity Score Matched SEER Analysis. Cancer research and treatment : official journal of Korean Cancer Association 2018.
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3. Hughes KS, et al. Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with early breast cancer. N Engl J Med. 2004 Sep 2;351(10):971-
4. Kunkler I, et al. Postoperative breast irradiation: new trials needed in older patients. J Clin Oncol. 2003 May 1;21(9):1893; author reply 1893-4
5. Fyles AW: Tamoxifen with or without breast irradiation in women 50 years of age or older with early breast cancer. N Engl J Med. 2004 Sep 2;351(10):963-70
6. Kunkler IH, Williams LJ, Jack WJ, et al: on behalf of the PRIME II investigators. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. Lancet Oncol. 2015 Jan 27.

Statement: Hypofractionated radiotherapy

1. Vaidya JS, Joseph DJ, Tobias JS et al: Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial. Lancet. 2010 Jul 10;376(9735):91-102.
2. Vaidya JS, Wenz F, Bulsara M, et al: TARGIT trialists' group. Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial. Lancet. 2014 Feb 15;383(9917):603-13.
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4. Ortholan C, et al. Long-term results of adjuvant hypofractionated radiotherapy for breast cancer in elderly patients. Int J Radiat Oncol Biol Phys. 2005 Jan 1;61(1):154-62.
5. Kirova YM, Campana F, Savignoni A, et al: for the Institut Curie Breast Cancer Study Group Breast-Conserving Treatment in the Elderly: Long-Term Results of Adjuvant Hypofractionated and Normofractionated Radiotherapy. Int J Radiat Oncol Biol Phys. 2009 Jan 2

Statement: No chemotherapy > 70 years and negative risk benefit analysis

1. Du XL, Jones DV, Zhang D. Effectiveness of adjuvant chemotherapy for node-positive operable breast cancer in older women. J

Gerontol A Biol Sci Med Sci. 2005 Sep;60(9):1137-44.

2. Kehl KL, Niu J, Chavez-MacGregor M et al. Hospitalization by cytotoxic chemotherapy regimen among older women with stage IV breast cancer. *Cancer* 2018;124(24):4685-91.
3. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005 May 14-20;365(9472):1687-717
4. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Adjuvant chemotherapy in oestrogen-receptor-poor breast cancer: patient-level meta-analysis of randomised trials. *Lancet*. 371;2008:1687-717

Mammakarzinom des Mannes: Diagnostik und lokale Therapie			
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ■ Diagnostische Aufarbeitung wie bei Frauen <ul style="list-style-type: none"> ■ Mammographie ■ Ultraschall ■ Standard-Op: Mastektomie <ul style="list-style-type: none"> ■ BET (Tumor-Brust-Relation!) ■ Sentinel-Node Biopsie (SNE) ■ Radiotherapie wie bei Frauen (beachte Tumor-Brust-Relation!) ■ Genetische Beratung, falls ein weiterer Verwandter / Verwandte betroffen ■ Krebsfrüherkennungsuntersuchungen gemäß Empfehlungen der DKG e.V. 	4 3b 2b 4 4 2b 4 2b GCP	C C B C C B C B	+ +/- ++ ++* +* + + ++ ++
* Teilnahme an Registerstudie empfohlen			

International registry

1. Cardoso F, Bartlett JMS, Slaets L et al. Characterization of male breast cancer: results of the EORTC 10085/TBCRC/BIG/NABCG International Male Breast Cancer Program. Ann Oncol 2018;29(2):405-17.
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General

1. Gucalp A, Traina TA, Eisner JR, Parker JS, Selitsky SR, Park BH, et al. Male breast cancer: a disease distinct from female breast cancer. Breast Cancer Res Treat 2018.
2. Fentiman IS. Unmet needs of men with breast cancer. Eur J Surg Oncol 2018;44(8):1123-26.

3. Vetto J et al. Accurate and cost-effective evaluation of breast masses in males. Am J Surg 1998 175: 3831.
4. Giordano SH. Breast Cancer in Men. N Engl J Med 2018;378(24):2311-20.
5. Kanakis GA, Jorgensen N, Goulis DG. Breast Cancer in Men. N Engl J Med 2018;379(14):1385.
6. Liu N, Johnson KJ, Ma CX. Male Breast Cancer: An Updated Surveillance, Epidemiology, and End Results Data Analysis. Clin Breast Cancer 2018;18(5):e997-e1002
7. Wang J, Sun Y, Qu J, Zuo H, Zhao X, Liu L, et al. Survival analysis for male ductal and lobular breast cancer patients with different stages. Future Oncol 2018.
8. Gucalp A, Traina TA, Eisner JR, Parker JS, Selitsky SR, Park BH, et al. Male breast cancer: a disease distinct from female breast cancer. Breast Cancer Res Treat 2018.
9. Wang K, Wang QJ, Xiong YF, Shi Y, Yang WJ, Zhang X, et al. Survival Comparisons Between Early Male and Female Breast Cancer Patients. Scientific reports 2018;8(1):8900.
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11. Thalib L ,Hall P. Survival of male breast cancer patients: Population-based cohort study. Cancer Sci. 2008
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13. Deb S, Lakhani SR, Ottini L, et al. The cancer genetics and pathology of male breast cancer. Histopathology. 2016 Jan;68(1):110-8.

Statement: Diagnostic work up as in women

Statement: Mammography

1. Chesebro AL, Rives AF, Shaffer K. Male Breast Disease: What the Radiologist Needs to Know. Current problems in diagnostic radiology 2018.
2. Dershaw DD. et al. Mammographic findings in men with breast cancer. Am J Roentgenol 1993 160: 267

3. Hines SL: The role of mammography in male patients with breast symptoms. Mayo Clin Proc. 2007 Mar;82(3):297-300

Statement: Ultrasound

1. Caruso G: High-frequency ultrasound in the study of male breast palpable masses. Radiol Med (Torino). 2004 Sep;108(3):185-93

Statement: Standard-surgery: Mastectomy – men

1. Shen. I et al Skin-sparing mastectomy: a survey based approach to defining standard of care. Am Surg. 2008 Oct;74(10):902-51.
2. Fentiman IS. Surgical options for male breast cancer. Breast Cancer Res Treat 2018;172(3):539-44.
3. Lanitis S et al. Diagnosis and management of male breast cancer, World J Surg. 2008 Nov;32(11):2471-6.
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5. Fogh S et al. Therapy for Male Breast Cancer: Functional Advantages With Comparable Outcomes Using Breast Conservation. Clin Breast Cancer. 2013;13(5):344-9.
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8. Zaenger D, Rabatic BM, Dasher B, Mourad WF. Is Breast Conserving Therapy a Safe Modality for Early-Stage Male Breast Cancer? Clin Breast Cancer. 2015 Nov 17. pii: S1526-8209(15)00278-5.

Statement: Sentinel-node excision (SNE)

1. Port ER et al. Sentinel lymph node biopsy in patients with male breast carcinoma. Cancer 2001 91:319-323
2. Flynn LW et al. Sentinel lymph node biopsy is successful and accurate in male breast carcinoma. J Am Coll Surg. 2008 Apr;206(4):616-21

3. Boughey JC: Comparative analysis of sentinel lymph node operation in male and female breast cancer patients. J Am Coll Surg. 2006 Oct;203(4):475-80. Epub 2006 Aug 23
4. De Cicco C: Sentinel node biopsy in male breast cancer. Nucl Med Commun 2004; 25: 139-143
5. Albo D et al. Evaluation of lymph node status in male breast cancer patients: a role for sentinel lymph node biopsy. Breast Cancer Res Treat 2003 77:9-14

Statement: Radiotherapy as in women (consider tumor breast relation!)

1. Ribeiro GG: A review of the management of the male breast carcinoma based on an analysis of 420 treated cases. Breast 1996; 5: 141-146
2. Schuchardt U et al. Adjuvant radiotherapy for breast carcinoma in men: a 20-year clinical experience. Am J Clin Oncol 1996 19:330
3. Eggemann H et al. Male breast cancer: 20-year survival data for post-mastectomy radiotherapy. Breast Care (Basel). 2013;8(4):270-5.

Statement: Genetic counselling if 1 additional relative affected (breast/ovarian cancer)

1. Ottini L et al. BRCA1/BRCA2 mutation status and clinical-pathologic features of 108 male breast cancer cases from Tuscany: a population-based study in central Italy. Breast Cancer Res Treat. 2008 Sep 26
2. Friedman LS, Gayther SA, Kurosaki T, et al. Mutation analysis of BRCA1 and BRCA2 in a male breast cancer population. Am J Hum Genet 1997; 60: 313-319
3. Basham VM: BRCA1 and BRCA2 mutations in a population-based study of male breast cancer. Breast Cancer Res 2002; 4: R2
4. Thorlacius S, Sigurdson S, Bjanadottir H, et al. Study of a single BRCA2 mutation with high carrier frequency in a small population. Am J Hum Genet 1997; 60: 1079-1084

Statement: Screening for 2nd malignancies according guidelines

1. Wernberg JA. Multiple primary tumors in men with breast cancer diagnoses: a SEER database review. J Surg Oncol. 2009 Jan

1;99(1):16-9

Statement: Systemic therapy


1. Doyen J et al., Ann Oncol. 2009 Oct 27. [Epub ahead of print], Aromatase inhibition in male breast cancer patients: biological and clinical implications.
2. Eggemann H et al. Adjuvant therapy with tamoxifen compared to aromatase inhibitors for 257 male breast cancer patients. Breast Cancer Res Treat. 2013;137(2):465-70.
3. Patten DK et al. New Approaches in the Management of Male Breast. Cancer Clinical Breast Cancer 2013;13(5) 309–314
4. Di Lauro L et al. Letrozole combined with gonadotropin-releasing hormone analog for metastatic male breast cancer Breast Cancer Res Treat. 2013;141(1):119-23
5. Zagouri F et al. Aromatase inhibitors with or without gonadotropin-releasing hormone analogue in metastatic male breast cancer: a case series. Br J Cancer. 2013;108(11):2259-63

Review articles

1. Donegan WL: Carcinoma of the breast in males. Cancer 1998; 83: 498-509
2. Borgen PI et al. Current management of male breast cancer. A review of 104 cases. Ann Surg 1992 215:451
3. Erlichman C et al. Male breast cancer: a 13- year review of 89 patients. J Clin Oncol 1984 2: 903
4. Cutuli B, Lacroze M, Dilhuydy JM, et al. Male breast cancer: results of the treatments and prognostic factors in 397 cases. Eur J Cancer 1995; 31A: 1960-1964
5. Fentiman IS, Fourquet A, Hortobagyi GN. Male breast cancer. Lancet. 2006 Feb 18;367(9510):595-604. Review. Erratum in: Lancet. 2006 Jun 3;367(9525):1818
6. Agrawal A, Ayantunde AA, Rampaul R et al. Male breast cancer: a review of clinical management. Breast Cancer Res Treat. 2006 Oct 11;
7. Korde LA et al: Multidisciplinary meeting on male breast cancer; summary and research recommendations J Clin Oncol 28: 2114-

2122, 2010

8. Patten DK et al. New Approaches in the Management of Male Breast. *Cancer Clinical Breast Cancer* 2013;13(5) 309–314
9. Sousa B et al. An update on male breast cancer and future directions for research and treatment. *Eur J Pharmacol* 2013;717(1-3)
10. Ruddy KJ et al. Male breast cancer: risk factors, biology, diagnosis, treatment, and survivorship. *Ann Oncol* 2013; 24(6):1434-43.



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in der DKG e.V.

Guidelines Breast
Version 2019.1D

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Mammakarzinom des Mannes: Systemtherapie

Oxford		
LoE	GR	AGO
2a	B	++
5	D	++
4	D	++
2b	B	++
2b	B	-
4	C	+/-
4	C	+*
4	C	+/-
4	C	++

- **Adjuvante Chemotherapie wie bei Frauen**
- **HER2 zielgerichtete Therapie (falls HER2 pos.)**
- **Endokrine Therapie bei HR pos.**
 - Tamoxifen
 - Aromataseinhibitoren (adjuvant)
 - Aromataseinhibitoren (metastasiert)
 - GnRHa + AI (metastasiert)
 - Fulvestrant (metastasiert)
- **Palliative Chemotherapie wie bei Frauen**

Statement: Adjuvant Chemotherapy

1. Patel HZ et al. Role of adjuvant chemotherapy in male breast cancer. Cancer 1989 64: 1583
2. Bagley CS et al. Adjuvant Chemotherapy in males with cancer of the breast. Am J Clin Oncol 1987; 2:903
3. Giordano SH, Perkins GH, Broglio K, et al. Adjuvant systemic therapy for male breast cancer. Cancer 2005; 104: 235-264
4. Walshe JM: A prospective study of adjuvant CMF in males with node positive breast cancer: 20-year follow-up. Breast Cancer Res Treat. 2007 Jun;103(2):177-83

Statement Trastuzumab

1. Carmona-Bayonas A. Potential benefit of maintenance trastuzumab and anastrozole therapy in male advanced breast cancer. Breast. 2007 Jun;16(3):323-5

Statement endocrine therapy


1. Ribeiro G et al. Adjuvant tamoxifen for male breast cancer (MBC). Br J Cancer 1992 65: 252

2. Anelli TF et al. Tamoxifen administration is associated with a high rate of treatment-limiting symptoms in male breast cancer patients. *Cancer* 1994 74: 74
3. Agrawal: Fulvestrant in advanced male breast cancer. *Breast Cancer Res Treat.* 2007 Jan;101(1):123. Epub 2006 Jun 29.
4. Zabolotny BP: Successful use of letrozole in male breast cancer: a case report and review of hormonal therapy for male breast cancer. *J Surg Oncol.* 2005 Apr 1; 90(1):26-30
5. Goss PE: Male breast carcinoma: a review of 229 patients who presented to the Princess Margaret Hospital during 40 years: 1955–1996. *Cancer* 1999; 85: 629-639
6. Giordano SH: Efficacy of anastrozole in male breast cancer. *Am J Clin Oncol* 2002 25: 235-237
7. Agrawal A: Fulvestrant in advanced male breast cancer. *Breast Cancer Res Treat.* 2007 Jan;101(1):123. Epub 2006 Jun 29. No abstract available
8. Giordano SH: Leuprolide acetate plus aromatase inhibition for male breast cancer. *J Clin Oncol.* 2006 Jul 20;24(21):e42-3. No abstract available.
9. Nahleh ZA: Hormonal therapy for male breast cancer: A different approach for a different disease. *Cancer Treatment Reviews* 2006 32:101-105
10. Arriola E: Aromatase inhibitors and male breast cancer. *Clin Transl Oncol.* 2007 Mar;9(3):192-4
11. Eggemann H, Ignatov A, Smith BJ, et al. Adjuvant therapy with tamoxifen compared to aromatase inhibitors for 257 male breast cancer patients. *Breast Cancer Res Treat.* 2013 Jan;137(2):465-70.
12. Di Lauro L et al. Letrozole combined with gonadotropin-releasing hormone analog for metastatic male breast cancer *Breast Cancer Res Treat.* 2013;141(1):119-23
13. Zagouri F et al. Aromatase inhibitors with or without gonadotropin-releasing hormone analogue in metastatic male breast cancer: a case series. *Br J Cancer.* 2013;108(11):2259-63

Statement palliative chemotherapy

1. Chitapanarux I: Gemcitabine plus cisplatin (GC): a salvage regimen for advanced breast cancer patients who have failed anthracycline

and/or taxane therapy. Gan To Kagaku Ryoho. 2006 Jun;33(6):761-6

 <p>AGO ARBEITSGEMEINSCHAFT GYNAKOLOGISCHE ONKOLOGIE e.V.</p> <p>MAMMA</p> <p>10-27-11-17</p>	<h2>Benefit from Trimodal Treatment in Inflammatory Breast Cancer</h2>		
<p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2019.1D</p>	Median survival probability		
	Trimodal therapy	72 months	p<0.05
	Surgery alone	26 months	
	Overall survival-probability (OS)		
		10 years-OS	5 years-OS
	Trimodal therapy	55.4%	37.3%
	Surgery & chemotherapy	42.9%	28.5%
	Surgery & radiotherapy	40.7%	23.5%
	Surgery alone		16.5%
	Multivariate analysis of OS		
		Hazard Ratio	95% CI
	Surgery & chemotherapy & RT (trimodal therapy)	1.00	-
	Surgery & chemotherapy	1.64	1.46 to 1.84
	Surgery & radiotherapy	1.47	0.96 to 2.24
	Surgery alone	2.28	1.80 to 2.89
<p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	<p>Rueth et al. J Clin Oncol 2014; 32:2018–2024</p>		

Survival benefit by trimodal treatment (NACT, MRM, RT)

1. Rueth NM, Lin HY, Bedrosian I, et al. Underuse of trimodality treatment affects survival for patients with inflammatory breast cancer: an analysis of treatment and survival trends from the National Cancer Database. *J Clin Oncol* 2014; **32**: 2018–24.

Primäres inflammatorisches Mammakarzinom (IBC, cT4d)			
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> Stadium cT4d definiert durch invasive Komponente in der Mamma und klinische Zeichen einer Inflammation (z.B. $\geq 1/3$ der betroffenen Brust) 			++
<ul style="list-style-type: none"> Staging 	2c	B	++
<ul style="list-style-type: none"> Hautbiopsie (mind. 2; Detektionsrate jedoch < 75%) 	2c	B	+
<ul style="list-style-type: none"> Neoadjuvante Chemotherapieregime (wie bei nicht inflammatorischem MaCA) 	2c	B	++
<ul style="list-style-type: none"> Leitliniengerechte Systemtherapie 	2c	B	++
<ul style="list-style-type: none"> Mastektomie nach Chemotherapie <ul style="list-style-type: none"> Brusterhaltende Therapie im Fall von pCR (Individualfall) Sentinel-Node-Biopsie 	2c	B	+
	2b	C	+/-
	3b	C	-
<ul style="list-style-type: none"> Radiotherapie der Brustwand 	2c	B	++



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General

- Ueno NT, Espinosa Fernandez JR, Cristofanilli M et al. International Consensus on the Clinical Management of Inflammatory Breast Cancer from the Morgan Welch Inflammatory Breast Cancer Research Program 10th Anniversary Conference. Journal of Cancer 2018;9(8):1437-47. 1.
- Audisio RA. Inflammatory Breast Cancer: Updates on diagnosis and treatment options. Eur J Surg Oncol 2018;44(8):1127.
- Copson E, Shaaban AM, Maishman T et al. The presentation, management and outcome of inflammatory breast cancer cases in the UK: Data from a multi-centre retrospective review. Breast 2018;42:133-41.
- Copson E, Shaaban AM, Maishman T et al. The presentation, management and outcome of inflammatory breast cancer cases in the UK: Data from a multi-centre retrospective review. Breast 2018;42:133-41.
- Romanoff A, Zabor EC, Petruolo O et al. Does nonmetastatic inflammatory breast cancer have a worse prognosis than other nonmetastatic T4 cancers? Cancer 2018;124(22):4314-21.
- Wu SG, Zhang WW, Wang J et al. Inflammatory breast cancer outcomes by breast cancer subtype: a population-based study. Future Oncol 2018.
- Brzezinska M, Williams LJ, Thomas J et al. Outcomes of patients with inflammatory breast cancer treated by breast-conserving

surgery. Breast Cancer Res Treat 2016;160(3):387-91.

8. Boudin L, Goncalves A, Sfumato P et al. Prognostic impact of hormone receptor- and HER2-defined subtypes in inflammatory breast cancer treated with high-dose chemotherapy: a retrospective study. Journal of Cancer 2016;7(14):2077-84.
9. Costa R, Santa-Maria CA, Rossi G et al. Developmental therapeutics for inflammatory breast cancer: Biology and translational directions. Oncotarget 2017;8(7):12417-32.
10. van Uden DJ, Bretveld R, Siesling S et al. Inflammatory breast cancer in the Netherlands; improved survival over the last decades. Breast Cancer Res Treat 2017;162(2):365-74.

In case of invasive BC and clinical signs of inflammation (e.g. $\geq 1/3$ of the breast affected) determine stage cT4d

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines(r)). Breast Cancer. Version 3.2018. NCCN.org (Inflammatory Breast Cancer. IBC-1)

Survival benefit by trimodal treatment (NACT, MRM, RT)

1. Rueth NM, Lin HY, Bedrosian I, et al. Underuse of trimodality treatment affects survival for patients with inflammatory breast cancer: an analysis of treatment and survival trends from the National Cancer Database. *J Clin Oncol* 2014; **32**: 2018–24.

Statement: Staging

1. Ueno NT, Espinosa Fernandez JR, Cristofanilli M et al. International Consensus on the Clinical Management of Inflammatory Breast Cancer from the Morgan Welch Inflammatory Breast Cancer Research Program 10th Anniversary Conference. Journal of Cancer 2018;9(8):1437-47.
2. Yamauchi H et al. Inflammatory breast cancer: what we know and what we need to learn. *Oncologist*. 2012;17(7):891-9. doi: 10.1634/theoncologist.2012-0039. Epub 2012 May 14.

3. S. Dawood et al International expert panel on inflammatory breast cancer: consensus statement for standardized diagnosis and treatment Ann Oncol. 2011 March; 22(3): 515–523
4. Chia S et al. Locally advanced and inflammatory breast cancer J Clin Oncol 2008; 26: 786-790

Statement: Preoperative chemotherapy

1. Ardavanis A: Multidisciplinary therapy of locally far-advanced or inflammatory breast cancer with fixed perioperative sequence of epirubicin, vinorelbine, and Fluorouracil chemotherapy, surgery, and radiotherapy: long-term results. Oncologist. 2006 Jun;11(6):563-73
2. S. Johnston (2008), J. Clin. Oncol. 26: 1066.1072
3. Mathew J et al. Neoadjuvant chemotherapy for locally advanced breast cancer : A review of the literature and future directions.
4. Schairer C et al. Risk factors for inflammatory breast cancer and other invasive breast cancers. J Natl Cancer Inst 2013;105:1373-84.
5. Van Laere et al. Uncovering the molecular secrets of inflammatory breast cancer biology: an integrated analysis of three distinct affymetrix gene expression datasets. Clin Cancer Res 2013;19:4685-96.

Statement: Regimens as in non-inflammatory BC

1. Chia S et al. Locally advanced and inflammatory breast cancer J Clin Oncol 2008; 26: 786-790

Statement: in HER2 positive disease addition of trastuzumab

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Axilla-Metastase(n) bei okkultem Mammakarzinom (Cancer of unknown primary – axillary CUP)

- **Inzidenz: < 1% aller axillären Metastasen**
- **In > 95% okkultes Mamma-Ca, in < 5% anderer Primarius**
- **Immunhistologie**
ER-positiv: 55%
HER2 3+: 35%
Triple-negativ: 38%
- **Nodalstatus:**
1–3 Lk-Met. in 48%
> 3 Lk-Met. in 52%
- **Outcome ähnlich oder besser als beim Mammakarzinom mit entsprechender Tumorbilogie und Stadium**

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Axilla-Metastasen bei okkultem Mammakarzinom (ax. CUP)

Bildgebende Diagnostik

	Oxford		
	LoE	GR	AGO
▪ Mammographie, Mamma-Ultraschall, Mamma-MRT	3	B	++
▪ Ausschluss eines kontralateralen Tumors	3	B	++
▪ Ausschluss eines anderen Organtumors insbes. bei TNBC (Haut, weibl. Genitaltrakt, Lunge, Schilddrüse, Magen)	5	D	++
▪ Staging (CT Thorax / Abdomen, Schilddrüsen- Sonographie, HNO-Untersuchung)	3	B	++
▪ PET / PET-CT	3b	B	+

Statement: Mammography / Breast ultrasound/ Breast MRI


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Statement: Staging

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Statement: PET

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Axilla-Metastasen bei okkultem Mammakarzinom (ax. CUP)

Pathologie, Molekularpathologie

	Oxford		
	LoE	GR	AGO
▪ ER, PgR, HER2, GATA3	5	D	++
▪ Ausschluss anderer Primärtumoren bei TNBC oder ungewöhnlicher Histologie, z. B. Lunge, weibl. Genitaltrakt, Kopf-Hals-Tumoren, neuroendokrine Ca	5	D	++
▪ Genexpressionsprofile zur Bestimmung des Primarius (z.B. CUPprint, Pathwork, TOT, Theros CTID)	2c	B	+/-
▪ NGS, Epigenetik zur Bestimmung des Primarius (Panel-Sequenzierung, z.B. EPICup)	2c	B	+/-
▪ Prognostische Genexpressionstests	5	D	--

Immunohistochemistry

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Axilla-Metastasen bei okkultem Mammakarzinom (ax. CUP)Therapie

	Oxford		
	LoE	GR	AGO
▪ Axilladisektion	3a	C	++
▪ Mastektomie bei unauffälligem MRT	3a	C	-
▪ Leitliniengerechte (neo-)adjuvante Systemtherapie	5	D	++
▪ Brust-Bestrahlung bei negativem Mamma-MRT	2c	B	+
▪ Bestrahlung der regionären LK	3b	B	+

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Statement: Axillary dissection

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Statement: Mastectomy without (in-)breast tumor

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Statement: Breast irradiation if breast MRI is negative

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Statement: Systemic treatment according N+ tumor

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M. Paget der Mamille

- **Beim M. Paget der Mamille handelt es sich um eine intraepidermale Manifestation eines intraduktalen oder eines invasiven Mammakarzinoms. Selten und meist tumorbiologisch weniger aggressiv ist der isolierte M. Paget.**


Merkmal	Häufigkeiten
Präsentation	M. Paget mit invasivem Ca. (37 – 58%) M. Paget mit DCIS (30 – 63%) Isolierter M. Paget (4 – 7%) Isolierter M. Paget mit Invasion (selten)
IHC	HER2-positiv (83 – 97%) ER-positiv (10 – 14%) AR-positiv (71 – 88%)

Clinical Presentation

1. Chen, C.-Y., Sun, L.-M., & Anderson, B. O. (2006). Paget disease of the breast: changing patterns of incidence, clinical presentation, and treatment in the U.S. *Cancer*, 107(7), 1448–1458. <http://doi.org/10.1002/cncr.22137>
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6. Siponen, E., Hukkinen, K., Heikkilä, P., et al. (2010). Surgical treatment in Paget's disease of the breast. *American Journal of Surgery*, 200(2), 241–246. <http://doi.org/10.1016/j.amjsurg.2009.07.044>

Pathology and Immunohistochemistry

1. Chen, C.-Y., Sun, L.-M., & Anderson, B. O. (2006). Paget disease of the breast: changing patterns of incidence, clinical presentation, and treatment in the U.S. *Cancer*, 107(7), 1448–1458. <http://doi.org/10.1002/cncr.22137>
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7. Schelfhout, V. R., Coene, E. D., Delaey, B., et al. (2000). Pathogenesis of Paget's disease: epidermal heregulin-alpha, motility factor, and the HER receptor family. *Journal of the National Cancer Institute*, 92(8), 622–628.



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Morbus Paget der Mamille

Diagnostik

Oxford		
LoE	GR	AGO
		++
4	D	++
4	C	+
5	D	++

- **Stanzbiopsische histologische Sicherung**
- **Mammographie, Mammasonographie**
- **Mamma-MR (falls andere Bildgebung nicht aussagekräftig)**
- **Immunhistologie (ER, PgR, HER2, Ck7) zur Abgrenzung benigner und HER2-negativer Befunde**


Imaging

1. Morrogh, M., Morris, E. A., Liberman, L. et al. (2008). MRI identifies otherwise occult disease in select patients with Paget disease of the nipple. Journal of the American College of Surgeons, 206(2), 316–321. <http://doi.org/10.1016/j.jamcollsurg.2007.07.046>
2. Günhan-Bilgen, I., & Oktay, A. (2006). Paget's disease of the breast: clinical, mammographic, sonographic and pathologic findings in 52 cases. European Journal of Radiology, 60(2), 256–263. <http://doi.org/10.1016/j.ejrad.2006.06.010>
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4. Moon, J. Y., Chang, Y.-W., Lee, E. H., et al. (2013). Malignant invasion of the nipple-areolar complex of the breast: usefulness of breast MRI. American Journal of Roentgenology, 201(2), 448–455. <http://doi.org/10.2214/AJR.12.9186>

Pathology

1. Sandoval-Leon, A. C., Drews-Elger, K., Gomez-Fernandez, C. R., et al. (2013). Paget's disease of the nipple. Breast Cancer Research and Treatment, 141(1), 1–12. <http://doi.org/10.1007/s10549-013-2661-4>

2. Saeed, D., & Shousha, S. (2014). Toker cells of the nipple are commonly associated with underlying sebaceous glands but not with lactiferous ducts. *Journal of Clinical Pathology*, 67(11), 1010–1012. <http://doi.org/10.1136/jclinpath-2014-202280>
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Morbus Paget der Mamille

Diagnostik

	Oxford		
	LoE	GR	AGO
▪ Morbus Paget mit Mamma-Tumor (invasives MaCa, DCIS)			
▪ Therapie entsprechend Standards der Grunderkrankung	5	D	++
▪ Operation mit R0 Resektion	1c	B	++
▪ Isolierter Morbus Paget des NAC:			
▪ R0-Resektion inkl. NAC	1c	B	++
▪ keine adjuvante Bestrahlung bei R0	4	D	++
▪ Sentinel-Lymphknoten-Exzision (SNE)	2b	B	--

Surgical Treatment of Pagets's disease associated with breast tumor (invasive carcinoma or DCIS)

1. Bijker, N., Rutgers, E. J., Duchateau, L., EORTC Breast Cancer Cooperative Group et al. (2001). Breast-conserving therapy for Paget disease of the nipple: a prospective European Organization for Research and Treatment of Cancer study of 61 patients. *Cancer*, 91(3), 472–477.
2. Caliskan, M., Gatti, G., Sosnovskikh, I., et al. (2008). Paget's disease of the breast: the experience of the European Institute of Oncology and review of the literature. *Breast Cancer Research and Treatment*, 112(3), 513–521. <http://doi.org/10.1007/s10549-007-9880-5>
3. Dalberg, K., Hellborg, H., & Wärnberg, F. (2008). Paget's disease of the nipple in a population based cohort. *Breast Cancer Research and Treatment*, 111(2), 313–319. <http://doi.org/10.1007/s10549-007-9783-5>
4. Dominici, L. S., Lester, S. C., Liao, G.-S., et al. (2012). Current surgical approach to Paget's disease. *American Journal of Surgery*, 204(1), 18–22. <http://doi.org/10.1016/j.amjsurg.2011.07.010>
5. Dominici, L. S., Lester, S. C., Liao, G.-S., et al. (2012). Current surgical approach to Paget's disease. *American Journal of Surgery*, 204(1), 18–22. <http://doi.org/10.1016/j.amjsurg.2011.07.01>
6. Laronga, C., Hasson, D., Hoover, S., et al. (2006). Paget's disease in the era of sentinel lymph node biopsy. *American Journal of*

Surgery, 192(4), 481–483. <http://doi.org/10.1016/j.amjsurg.2006.06.023>


7. Siponen, E., Hukkinen, K., Heikkilä, P., et al. (2010). Surgical treatment in Paget's disease of the breast. American Journal of Surgery, 200(2), 241–246. <http://doi.org/10.1016/j.amjsurg.2009.07.044>

Treatment of isolated Paget's disease

1. Durkan, B., Bresee, C., Bose, S. et al. (2013). Paget's disease of the nipple with parenchymal ductal carcinoma in situ is associated with worse prognosis than Paget's disease alone. The American Surgeon, 79(10), 1009–1012.
2. Lagios, M. D., Westdahl, P. R., Rose, M. R. et al. (1984). Paget's disease of the nipple. Alternative management in cases without or with minimal extent of underlying breast carcinoma. Cancer, 54(3), 545–551.
3. Mirer, E., Sayed, El, F., Ammourey, A., et al. (2006). Treatment of mammary and extramammary Paget's skin disease with topical imiquimod. The Journal of Dermatological Treatment, 17(3), 167–171. <http://doi.org/10.1080/09546630600788877>

Statement: Sentinel-node excision (SNE)

1. Bijker, N., Rutgers, E. J., Duchateau, L EORTC Breast Cancer Cooperative Group et al. (2001). Breast-conserving therapy for Paget disease of the nipple: a prospective European Organization for Research and Treatment of Cancer study of 61 patients. Cancer, 91(3), 472–477.



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Borderline und maligner Phylloidentumor

- Differenzialdiagnose gegenüber anderen Läsionen an der Stanzbiopsie problematisch
- Intramammäres Rezidiv relativ häufig (10 – 30%)
- Fernmetastasierung insgesamt selten (< 10%) und fast ausschließlich beim malignen Phylloidentumor

Merkmal	Häufigkeiten
Grading	Benigne (75%) Borderline (16%) Maligne (9%)
Medianes Alter bei Diagnosestellung	Benigner PT: 39 J. Borderline PT: 45 J. Maligner PT: 47 J.
Lokalrezidive	Benigner PT: 10 – 17% Borderline PT: 14 – 25% Maligner PT: 23 – 30%


Review

1. Tan, B. Y., Acs, G., Apple, S. K et al. (2016). Phyllodes tumours of the breast: a consensus review. Histopathology, 68(1), 5–21. <http://doi.org/10.1111/his.12876>

Pathology and Outcome

1. Barrio, A., Clark, B., Goldberg, J. et al. (2007). Clinicopathologic Features and Long-Term Outcomes of 293 Phyllodes Tumors of the Breast. Annals of Surgical Oncology.
2. Chaney, A. W., Pollack, A., McNeese, M. D., et al. (2000). Primary treatment of cystosarcoma phyllodes of the breast. Cancer, 89(7), 1502–1511.
3. Esposito, N. N., Mohan, D., Brufsky, A., et al. (2006). Phyllodes tumor: a clinicopathologic and immunohistochemical study of 30 cases. Archives of Pathology & Laboratory Medicine, 130(10), 1516–1521. [http://doi.org/10.1043/1543-2165\(2006\)130\[1516:PTACAI\]2.0.CO;2](http://doi.org/10.1043/1543-2165(2006)130[1516:PTACAI]2.0.CO;2)
4. Roa, J. C., Tapia, O., Carrasco, P., et al. (2006). Prognostic factors of phyllodes tumor of the breast. Pathology International, 56(6), 309–314. <http://doi.org/10.1111/j.1440-1827.2006.01965.x>

5. Tan, P. H., Jayabaskar, T., Chuah, K.-L. et al. (2005). Phyllodes tumors of the breast: the role of pathologic parameters. *American Journal of Clinical Pathology*, 123(4), 529–540. <http://doi.org/10.1309/U6DV-BFM8-1MLJ-C1FN>
6. Tan, P. H., Thike, A. A., Tan, W. J., et al. (2012). Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins. *Journal of Clinical Pathology*, 65(1), 69–76. <http://doi.org/10.1136/jclinpath-2011-200368>



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Borderline und maligner Phylloides tumor Diagnostik

	Oxford		
	LoE	GR	AGO
■ Mammographie / Mamma-Ultraschall (MG / MS)	3	C	++
■ Stanzbiopsische Diagnostik des PT, Dignitäts- beurteilung am Resektat	3	C	++
■ Mamma-MR	3	C	+/-
■ Staging nur beim malignen PT (CT Thorax, Knochen)	5	D	++

Imaging

1. Plaza, M. J., Swintelski, C., Yaziji, H., et al. (2015). Phyllodes tumor: review of key imaging characteristics. *Breast Disease*, 35(2), 79–86. <http://doi.org/10.3233/BD-150399>
2. Kamitani, T., Matsuo, Y., Yabuuchi, H., et al. (2014). Differentiation between benign phyllodes tumors and fibroadenomas of the breast on MR imaging. *European Journal of Radiology*, 83(8), 1344–1349. <http://doi.org/10.1016/j.ejrad.2014.04.031>
3. Liberman, L., Bonaccio, E., Hamele-Bena, D. et al. (1996). Benign and malignant phyllodes tumors: mammographic and sonographic findings. *Radiology*, 198(1), 121–124. <http://doi.org/10.1148/radiology.198.1.8539362>

Core biopsy

1. Abdulcadir, D., Nori, J., Meattini, I., et al. (2014). Phyllodes tumours of the breast diagnosed as B3 category on image-guided 14-gauge core biopsy: analysis of 51 cases from a single institution and review of the literature. *European Journal of Surgical Oncology* 40(7), 859–864. <http://doi.org/10.1016/j.ejso.2014.02.222>
2. Dillon, M., Quinn, C., McDermott, E., et al. (2006). Needle core biopsy in the diagnosis of phyllodes neoplasm. *Surgery*, 140(5), 779–784.

3. Jacobs, T., Chen, Y., Guinee, D., et al. (2005). Fibroepithelial lesions with cellular stroma on breast core needle biopsy: are there predictors of outcome on surgical excision? *American Journal of Clinical Pathology*, 124(3), 342–354.
4. Jara-Lazaro, A. R., Akhilesh, M., Thike, A. A., et al. (2010). Predictors of phyllodes tumours on core biopsy specimens of fibroepithelial neoplasms. *Histopathology*, 57(2), 220–232. <http://doi.org/10.1111/j.1365-2559.2010.03607.x>
5. Jung, H. K., Moon, H. J., Kim, M. J., et al. (2014). Benign core biopsy of probably benign breast lesions 2 cm or larger: correlation with excisional biopsy and long-term follow-up. *Ultrasonography (Seoul, Korea)*, 33(3), 200–205. <http://doi.org/10.14366/usg.14011>



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Operative Therapie

	Oxford		
	LoE	GR	AGO
▪ R0-Resektion mit Randabstand von mind. 5mm unabh. vom Grading	2b	B	++
▪ SNE / Axilladisektion bei cN0	4	C	--
▪ Therapie des Lokalrezidivs			
▪ R0-Resektion oder einfache Mastektomie	4	C	++

Statement: Complete (wide) local excision or MRM

Surgical margins

1. Guillot, E., Couturaud, B., Rey, F., et al. (2011). Management of phyllodes breast tumors. Breast Journal, 17(2), 129–137. <http://doi.org/10.1111/j.1524-4741.2010.01045.x>
2. Onkendi, E. O., Jimenez, R. E., Spears, G. M., et al. (2014). Surgical treatment of borderline and malignant phyllodes tumors: the effect of the extent of resection and tumor characteristics on patient outcome. Annals of Surgical Oncology, 21(10), 3304–3309. <http://doi.org/10.1245/s10434-014-3909-x>
3. Lin, C.-C., Chang, H.-W., Lin, C.-Y., et al. (2013). The clinical features and prognosis of phyllodes tumors: a single institution experience in Taiwan. International Journal of Clinical Oncology, 18(4), 614–620. <http://doi.org/10.1007/s10147-012-0442-4>
4. Yom, C. K., Han, W., Kim, S.-W., et al. (2015). Reappraisal of conventional risk stratification for local recurrence based on clinical outcomes in 285 resected phyllodes tumors of the breast. Annals of Surgical Oncology, 22(9), 2912–2918. <http://doi.org/10.1245/s10434-015-4395-5>
5. Mituś, J., Reinfuss, M., Mituś, J. W., et al. (2014). Malignant phyllodes tumor of the breast: treatment and prognosis. Breast

Journal, 20(6), 639–644. <http://doi.org/10.1111/tbj.12333>

6. Co M., Chen C., Tsang JY., et al. (2018). Mammary phyllodes tumour: a 15 year multicentre clinical review. *J Clin Pathol.*, 71(6):493-497. doi: 10.1136/jclinpath-2017-204827.
7. Adam MJ, Bendifallah S, Kalhorpour N et al. (2018). Time to revise classification of phyllodes tumor of the breast? Results of a French multicentric study. *Eur J Surg Oncol*, 44(11), 1743-1749. doi: 10.1016/j.esjo.2018.08.007

Operative management and prognosis of Phyllodes Tumors

1. Macdonald, O. K., Lee, C. M., Tward, J. D., et al. (2006). Malignant phyllodes tumor of the female breast: association of primary therapy with cause-specific survival from the Surveillance, Epidemiology, and End Results (SEER) program. *Cancer*, 107(9), 2127–2133. <http://doi.org/10.1002/cncr.22228>
2. Fou, A., Schnabel, F. R., Hamele-Bena, D., et al. (2006). Long-term outcomes of malignant phyllodes tumors patients: an institutional experience. *American Journal of Surgery*, 192(4), 492–495. <http://doi.org/10.1016/j.amjsurg.2006.06.017>
3. Cheng, S.-P., Chang, Y.-C., Liu, T.-P., Lee, J.-J., Tzen, C.-Y., & Liu, C.-L. et al (2006). Phyllodes tumor of the breast: the challenge persists. *World Journal of Surgery*, 30(8), 1414–1421. <http://doi.org/10.1007/s00268-005-0786-2>
4. Ben Hassouna, J., Damak, T., Gamoudi, A., et al. (2006). Phyllodes tumors of the breast: a case series of 106 patients. *American Journal of Surgery*, 192(2), 141–147. <http://doi.org/10.1016/j.amjsurg.2006.04.007>
5. Pezner, R. D., Schultheiss, T. E., & Paz, I. B. (2008). Malignant phyllodes tumor of the breast: local control rates with surgery alone. *International Journal of Radiation Oncology, Biology, Physics*, 71(3), 710–713. <http://doi.org/10.1016/j.ijrobp.2007.10.051>
6. Mituś, J., Reinfuss, M., Mituś, J. W., et al. (2014). Malignant phyllodes tumor of the breast: treatment and prognosis. *Breast Journal*, 20(6), 639–644. <http://doi.org/10.1111/tbj.12333>
7. Mishra, S. P., Tiwary, S. K., Mishra, M., et al. (2013). Phyllodes tumor of breast: a review article. *ISRN Surgery*, 2013(3), 361469–10. <http://doi.org/10.1155/2013/361469>
8. Soumarová, R., Šeneklová, Z., Horová, H., et al. (2004). Retrospective analysis of 25 women with malignant cystosarcoma phyllodes--treatment results. *Archives of Gynecology and Obstetrics*, 269(4), 278–281. <http://doi.org/10.1007/s00404-003-0593-7>

Statement: SNE / Axillary dissection in cNO

1. Mishra, S. P., Tiwary, S. K., Mishra, M., et al. (2013). Phyllodes tumor of breast: a review article. *ISRN Surgery*, 2013(3), 361469–10. <http://doi.org/10.1155/2013/361469>
2. Chen, W.-H., Cheng, S.-P., Tzen, C.-Y. et al. (2005). Surgical treatment of phyllodes tumors of the breast: retrospective review of 172 cases. *Journal of Surgical Oncology*, 91(3), 185–194. <http://doi.org/10.1002/jso.20334>
3. Kim, Y.-J., & Kim, K. (2017). Radiation therapy for malignant phyllodes tumor of the breast: An analysis of SEER data. *Breast (Edinburgh, Scotland)*, 32, 26–32. <http://doi.org/10.1016/j.breast.2016.12.006>

Statement: Staging

1. Tan, B. Y., Acs, G., Apple, S. K., et al. (2016). Phyllodes tumours of the breast: a consensus review. *Histopathology*, 68(1), 5–21. <http://doi.org/10.1111/his.12876>
2. Belkacémi, Y., Bousquet, G., Marsiglia, H., et al. (2008). Phyllodes tumor of the breast. *International Journal of Radiation Oncology, Biology, Physics*, 70(2), 492–500. <http://doi.org/10.1016/j.ijrobp.2007.06.059>

Statements: Systemic adjuvant therapy/ Chemotherapy and Endocrine therapy

1. Soumarová, R., Šeneklová, Z., Horová, H., et al. (2004). Retrospective analysis of 25 women with malignant cystosarcoma phyllodes--treatment results. *Archives of Gynecology and Obstetrics*, 269(4), 278–281. <http://doi.org/10.1007/s00404-003-0593-7>
2. Tan, E. Y., Tan, P. H., Hoon, T. P., et al. (2006). Recurrent phyllodes tumours of the breast: pathological features and clinical implications. *ANZ J Surg*, 76(6), 476–480. <http://doi.org/10.1111/j.1445-2197.2006.03754.x>
3. Chaney, A. W., Pollack, A., McNeese, M. D., et al. (2000). Primary treatment of cystosarcoma phyllodes of the breast. *Cancer*, 89(7), 1502–1511.
4. Chen, W.-H., Cheng, S.-P., Tzen, C.-Y., et al. (2005). Surgical treatment of phyllodes tumors of the breast: retrospective review of 172 cases. *Journal of Surgical Oncology*, 91(3), 185–194. <http://doi.org/10.1002/jso.20334>
5. Morales-Vásquez, F., Gonzalez-Angulo, A. M., Broglio, K., et al. (2007). Adjuvant chemotherapy with doxorubicin and dacarbazine has

no effect in recurrence-free survival of malignant phyllodes tumors of the breast. *The Breast Journal*, 13(6), 551–556. <http://doi.org/10.1111/j.1524-4741.2007.00510.x>

6. Spitaleri, G., Toesca, A., Botteri, E. et al. (2013). Breast phyllodes tumor: a review of literature and a single center retrospective series analysis. *Critical Reviews in Oncology/Hematology*, 88(2), 427–436. <http://doi.org/10.1016/j.critrevonc.2013.06.005>

Statement: Adjuvant radiotherapy, if T ≥2cm (BCT) or T ≥10cm (mastectomy)

1. Kim, Y.-J., & Kim, K. (2017). Radiation therapy for malignant phyllodes tumor of the breast: An analysis of SEER data. *Breast (Edinburgh, Scotland)*, 32, 26–32. <http://doi.org/10.1016/j.breast.2016.12.006>
2. Gnerlich, J. L., Williams, R. T., Yao, K., et al. (2014). Utilization of radiotherapy for malignant phyllodes tumors: analysis of the National Cancer Data Base, 1998-2009. *Annals of Surgical Oncology*, 21(4), 1222–1230. <http://doi.org/10.1245/s10434-013-3395-6>
3. Barth, R. J., Wells, W. A., Mitchell, S. E., et al. (2009). A prospective, multi-institutional study of adjuvant radiotherapy after resection of malignant phyllodes tumors. *Annals of Surgical Oncology*, 16(8), 2288–2294. <http://doi.org/10.1245/s10434-009-0489-2>
4. Belkacémi, Y., Bousquet, G., Marsiglia, H. et al. (2008). Phyllodes tumor of the breast. *International Journal of Radiation Oncology, Biology, Physics*, 70(2), 492–500. <http://doi.org/10.1016/j.ijrobp.2007.06.059>
5. Mituś, J., Reinfuss, M., Mituś, J. W., Jakubowicz, J., Blecharz, P., Wysocki, W. M., & Skotnicki, P. (2014). Malignant phyllodes tumor of the breast: treatment and prognosis. *Breast Journal*, 20(6), 639–644. <http://doi.org/10.1111/tbj.12333>
6. Choi, N., Kim, K., Shin, K.H., et al. (2018). [Malignant and borderline phyllodes tumors of the breast: a multicenter study of 362 patients \(KROG 16-08\)](#). *Breast Cancer Res Treat.* 2018 Sep;171(2):335-344. doi: 10.1007/s10549-018-4838-3. Epub 2018 May 28.

Statement: Treatment of local recurrence => R0 Resection: References (retrospective analysis , case reports)

1. Soumarová, R., Šeneklová, Z., Horová, H. et al. (2004). Retrospective analysis of 25 women with malignant cystosarcoma phyllodes--treatment results. *Archives of Gynecology and Obstetrics*, 269(4), 278–281. <http://doi.org/10.1007/s00404-003-0593-7>
2. Tan, E. Y., Tan, P. H., Hoon, T. P., et al. (2006). Recurrent phyllodes tumours of the breast: pathological features and clinical

implications. ANZ J Surg, 76(6), 476–480. <http://doi.org/10.1111/j.1445-2197.2006.03754.x>

3. Mituś, J., Reinfuss, M., Mituś, J. W., et al. (2014). Malignant phyllodes tumor of the breast: treatment and prognosis. Breast Journal, 20(6), 639–644. <http://doi.org/10.1111/tbj.12333>

Statement: Radiotherapy, chemotherapy after R1 resection

Statement: Distant metastases (very rare) => Treatment like soft tissue sarcomas


1. Jardim, D. L. F., Conley, A., & Subbiah, V. (2013). Comprehensive characterization of malignant phyllodes tumor by whole genomic and proteomic analysis: biological implications for targeted therapy opportunities. Orphanet Journal of Rare Diseases, 8(1), 112. <http://doi.org/10.1186/1750-1172-8-112>
2. Wang, H., Wang, X., & Wang, C.-F. (2014). Comparison of clinical characteristics between benign borderline and malignant phyllodes tumors of the breast. Asian Pacific Journal of Cancer Prevention : APJCP, 15(24), 10791–10795. <http://doi.org/10.7314/APJCP.2014.15.24.10791>

Borderline und maligner Phylloides tumor Adjuvante Therapie

	Oxford		
	LoE	GR	AGO
▪ Adjuvante Radiotherapie bei T \geq 2 cm (BEO) oder T \geq 10 cm (Mastektomie)	4 2b	C C	-- +/-
▪ Systemische adjuvante Therapie (Chemotherapie, endokrine Therapie)	4	C	--
▪ Therapie des Lokalrezidivs			
▪ R0-Resektion oder einfache Mastektomie	4	C	+
▪ Radiotherapie, Chemotherapie nach R1-Resektion	4	C	+/-
▪ Fernmetastasen (sehr selten)			
▪ Therapie wie bei Weichteilsarkomen	4	C	++

Sarkome der Mamma

- **Nicht selten assoziiert mit familiären Syndromen (Li-Fraumeni, Familiäre Adenomatöse Polyposis, Neurofibromatose Typ 1)**
- **Primäre Sarkome: Angiosarkom, undifferenziertes Sarkom, Leiomyosarkom, Liposarkom, Osteosarkom**
- **Sekundäre Malignome der Mamma:**
 - Radiotherapie-assoziierte Angiosarkome
 - Brust-Implantat-assoziierte großzellig-anaplastische Lymphome (BI-ALCL)
- **Selten: Intramammäre Sarkommetastasen**
- **Staging: TNM (UICC) bzw. AJCC-Schema der Weichteilsarkome analog anwendbar für Sarkome der Mamma**
- **Grading: Analog zum FNCLCC-System für Sarkome bzw. nach Rosen (1988) für Angiosarkome**



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Primäres Angiosarkom der Mamma

- **Häufigstes primäres Sarkom der Mamma**
- **Junges Alter (Median: 24 – 46 J.)**
- **Unschärfe Raumforderung**
- **Großer Tumor (Median: 5 – 7 cm)**
- **Untypischer Mammographie- und Sonographiebefund**
- **Hohes Lokalrezidivrisiko, auch nach Mastektomie**
- **Ungünstigere Prognose als andere primäre Sarkome der Mamma**

Reviews

1. Depla, A. L., Scharloo-Karels, C. H., de Jong, M. A. A., et al. (2014). Treatment and prognostic factors of radiation-associated angiosarcoma (RAAS) after primary breast cancer: a systematic review. *European Journal of Cancer*, 50(10), 1779–1788. <http://doi.org/10.1016/j.ejca.2014.03.002>
2. Kaklamanos, I. G., Birbas, K., Syrigos, K. N., et al. (2011). Breast angiosarcoma that is not related to radiation exposure: a comprehensive review of the literature. *Surgery Today*, 41(2), 163–168. <http://doi.org/10.1007/s00595-010-4341-x>
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8. Hodgson, N. C., Bowen-Wells, C., Moffat, F. et al. (2007). Angiosarcomas of the breast: a review of 70 cases. *American Journal of Clinical Oncology*, 30(6), 570–573. <http://doi.org/10.1097/COC.0b013e3181131d62>
9. Kunkiel, M., Maczkiewicz, M., Jagiello-Grusfeld, A., et al. (2018). Primary angiosarcomas of the breast-series of 11 consecutive cases-a single centre experience. [Curr Oncol.](#), 25(1):e50-e53. doi: 10.3747/co.25.3816. Epub 2018 Feb 28.



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Primäres Angiosarkom der Brust*

Diagnostik

Oxford		
LoE	GR	AGO
3a	C	--
3a	C	++
3a	C	++
3a	C	--
4	D	++
3a	C	++

- **MG/ MS zur Bestimmung der Tumorausdehnung**
- **Präop. MRT zur Bestimmung der Tumorausdehnung**
- **Diagnose durch Stanzbiopsie**
- **Diagnose durch Feinnadelbiopsie**
- **Staging (CT Thorax, Abd.; bei Angiosarkom MRI Kopf)**
- **Prognostische Faktoren:**
Größe, Grading, Tumorränder

* Behandlung in spezialisierten Zentren empfohlen

Imaging

1. Glazebrook, K. N., Magut, M. J., & Reynolds, C. (2008). Angiosarcoma of the breast. American Journal of Roentgenology, 190(2), 533–538. <http://doi.org/10.2214/AJR.07.2909>
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Pathology

1. Nascimento, A. F., Raut, C. P., & Fletcher, C. D. M. (2008). Primary angiosarcoma of the breast: clinicopathologic analysis of 49 cases, suggesting that grade is not prognostic. The American Journal of Surgical Pathology, 32(12), 1896–1904.

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Prognostic Factors

1. Wang, L., Lao, I. W., Yu, L., et al. (2016). Primary Breast Angiosarcoma: A Retrospective Study of 36 Cases from a Single Chinese Medical Institute with Clinicopathologic and Radiologic Correlations. *Breast Journal*. <http://doi.org/10.1111/tbj.12731>
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3. Vorburger, S., Xing, Y., Hunt, K., et al. (2005). Angiosarcoma of the breast. *Cancer*, 104(12), 2682–2688. <http://doi.org/10.1002/cncr.21531>
4. [Gervais, M.K.](#), [Burtenshaw, S.M.](#), [Maxwell, J.](#) et al. (2017). **Clinical outcomes in breast angiosarcoma patients: A rare tumor with unique challenges.** [J Surg Oncol](#). 2017 Dec;116(8):1056-1061. doi: 10.1002/jso.24780. Epub 2017 Dec 4.



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Primäres Angiosarkom der Brust*

Therapie

Oxford		
LoE	GR	AGO
3a	C	++
3a	C	-
3a	C	--
4	C	+/-
4	C	+/-

- Operation mit weiten freien Tumorrändern, i.d.R. Mastektomie
 - Brusterhaltende Therapie
- SNB oder axilläre Dissektion im Falle cN0
- Adjuvante Chemotherapie (Anthrazyklin/Taxan-basiert)
- Adjuvante Radiotherapie, wenn high risk (Größe > 5 cm, R1)

* Behandlung in spezialisierten Zentren empfohlen


Surgery

- Hui, A., Henderson, M., Speakman, D., et al. (2012). Angiosarcoma of the breast: a difficult surgical challenge. Breast (Edinburgh, Scotland), 21(4), 584–589. <http://doi.org/10.1016/j.breast.2012.01.001>
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- Vorburger, S., Xing, Y., Hunt, K. et al. (2005). Angiosarcoma of the breast. Cancer, 104(12), 2682–2688. <http://doi.org/10.1002/cncr.21531>

Adjuvant Treatment (Chemotherapy, Radiotherapy)

- Ghareeb, E. R., Bhargava, R., Vargo, J. A., et al. (2016). Primary and Radiation-induced Breast Angiosarcoma: Clinicopathologic Predictors of Outcomes and the Impact of Adjuvant Radiation Therapy. American Journal of Clinical Oncology, 39(5), 463–467. <http://doi.org/10.1097/COC.0000000000000077>
- Young, R. J., Fernando, M., Hughes, D et al. (2014). Angiogenic growth factor expression in benign and malignant vascular tumours. Experimental and Molecular Pathology, 97(1), 148–153. <http://doi.org/10.1016/j.yexmp.2014.06.010>

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Sekundäres (Radiotherapie-assoziiertes) Angiosarkom der Mamma

- **Kumulative Inzidenz des Radiotherapie-assoziierten Sarkoms:
3.2 per 1,000 nach 15 Jahren**
- **Klinische Präsentation**
 - > 5 Jahre nach BET oder Ablatio mit Nachbestrahlung
 - meist intrakutan oder subkutan im Bestrahlungsgebiet mit lividen Hauteffloreszenzen,
 - multiple Herde
 - häufig im fortgeschrittenen Stadien (II – III)
 - Metastasen meist pulmonal, Lymphknoten möglich
- **Prognose ungünstiger als bei Nicht-Radiotherapie assoziierten Sarkomen**
- **Überleben nach 5 Jahren: 15%**

1. Shah, S., & Rosa, M. (2016). Radiation-Associated Angiosarcoma of the Breast: Clinical and Pathologic Features. Archives of Pathology & Laboratory Medicine, 140(5), 477–481. <http://doi.org/10.5858/arpa.2014-0581-RS>
2. Depla, A. L., Scharloo-Karels, C. H., de Jong, M. A. A., et al. (2014). Treatment and prognostic factors of radiation-associated angiosarcoma (RAAS) after primary breast cancer: a systematic review. European Journal of Cancer (Oxford, England : 1990), 50(10), 1779–1788. <http://doi.org/10.1016/j.ejca.2014.03.002>
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5. Sheth, G. R., Cranmer, L. D., Smith, B. D., et al. (2012). Radiation-induced sarcoma of the breast: a systematic review. The Oncologist, 17(3), 405–418. <http://doi.org/10.1634/theoncologist.2011-0282>
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9. Nestle-Krämling, C., Bölke, E., Budach, W., et al. (2011). Hämangiosarkom nach brusterhaltender Therapie beim Mammakarzinom: vier Fallbeispiele mit molekulargenetischer Diagnostik und Literaturübersicht. *Strahlenther Onkol*, 187(10), 656–664. <http://doi.org/10.1007/s00066-011-2251-5>
10. Dogan, A., Kern, P., Schultheis, B. et al. (2018). Radiogenic angiosarcoma of the breast: case report and systematic review of the literature. *BMC Cancer*, 24;18(1):463. doi: 10.1186/s12885-018-4369-7.



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Sekundäres Angiosarkom der Brust Therapie

Oxford		
LoE	GR	AGO
3a	C	++
2b	B	+/-
2b	B	+/-
2b	B	+/-

- Sekundäre Mastektomie
- Adjuvante Chemotherapie (Anthrazyklin/Taxan-basiert)
- Adjuvante Radiotherapie bei Hochrisiko (Größe > 5 cm, R1)
- Regionale Hyperthermie (Verbesserung lokale Kontrolle) plus Chemotherapie und/oder Radiotherapie

Surgery

1. Lindford, A., Böhling, T., Vaalavirta, L., et al. (2011). Surgical management of radiation-associated cutaneous breast angiosarcoma. Journal of Plastic, Reconstructive & Aesthetic Surgery : JPRAS, 64(8), 1036–1042. <http://doi.org/10.1016/j.bjps.2011.02.014>
2. Jallali, N., James, S., Searle, A., et al. (2012). Surgical management of radiation-induced angiosarcoma after breast conservation therapy. American Journal of Surgery, 203(2), 156–161. <http://doi.org/10.1016/j.amjsurg.2010.12.011>

Adjuvant Chemotherapy

1. Jallali, N., James, S., Searle, A., et al. (2012). Surgical management of radiation-induced angiosarcoma after breast conservation therapy. American Journal of Surgery, 203(2), 156–161. <http://doi.org/10.1016/j.amjsurg.2010.12.011>
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3. Azzariti, A., Porcelli, L., Mangia, A., et al. (2014). Irradiation-induced angiosarcoma and anti-angiogenic therapy: a therapeutic hope? Exp Cell Res, 321(2), 240–247. <http://doi.org/10.1016/j.yexcr.2013.12.018>

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6. Penel, N., Bui, B. N., Bay, J.-O., et al. (2008). Phase II trial of weekly paclitaxel for unresectable angiosarcoma: the ANGIOTAX Study. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology*, 26(32), 5269–5274. <http://doi.org/10.1200/JCO.2008.17.3146>
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Adjuvant Radiotherapy

1. Ghareeb, E. R., Bhargava, R., Vargo, J. A. et al. (2016). Primary and Radiation-induced Breast Angiosarcoma: Clinicopathologic Predictors of Outcomes and the Impact of Adjuvant Radiation Therapy. *American Journal of Clinical Oncology*, 39(5), 463–467. <http://doi.org/10.1097/COC.0000000000000077>
2. Palta, M., Morris, C. G., Grobmyer, S. R., et al. (2010). Angiosarcoma after breast-conserving therapy. *Cancer*, 116(8), 1872–1878. <http://doi.org/10.1002/cncr.24995>
3. Sheth, G. R., Cranmer, L. D., Smith, B. D., et al. (2012). Radiation-induced sarcoma of the breast: a systematic review. *The Oncologist*, 17(3), 405–418. <http://doi.org/10.1634/theoncologist.2011-0282>
4. Müller, A.-C., Eckert, F., Heinrich, V. et al. (2011). Re-surgery and chest wall re-irradiation for recurrent breast cancer: a second curative approach. *BMC Cancer*, 11(1), 197. <http://doi.org/10.1186/1471-2407-11-197>

Adjuvant Hyperthermia

1. Lim, S. Z., Ong, K. W., Tan, B. K. T., et al. (2016). Sarcoma of the breast: an update on a rare entity. *Journal of Clinical Pathology*, 69(5), 373–381. <http://doi.org/10.1136/jclinpath-2015-203545>

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 3. Linthorst, M., van Geel, A. N., Baartman, E. A., et al. (2013). Effect of a combined surgery, re-irradiation and hyperthermia therapy on local control rate in radio-induced angiosarcoma of the chest wall. *Strahlenther Onkol*, 189(5), 387–393. <http://doi.org/10.1007/s00066-013-0316-3>
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 5. Sauer, R., Creeze, H., Hulshof, M., et al. Interdisciplinary Working Group for Clinical Hyperthermia (Atzelsberg Circle) of the German Cancer Society and the German Society of Radiooncology. (2012). Concerning the final report “Hyperthermia: a systematic review” of the Ludwig Boltzmann Institute for Health Technology Assessment, Vienna, March 2010. *Strahlenther Onkol*, 188(3), 209–213. <http://doi.org/10.1007/s00066-012-0072-9>
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1. Strobbe LJ, Peterse HL, van Tinteren H. Angiosarcoma of the breast after conservation therapy for invasive cancer. The incidence and outcome. *Breast Cancer Res Treat* 1998; 47: 101-109.
 2. Barrow BJ, Janjan NA, Gutman H, et al. Role of radiotherapy in sarcoma of the breast- a retrospective review of the M.D. Anderson experience. *Radiother Oncol*. 1999;52(2):173-8
 3. Huang J, Mackillop WJ. Increased risk of soft tissue sarcoma after radiotherapy in women with breast carcinoma. *Cancer* 2001; 92: 172-180



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Angiosarkome der Brust

Therapie von Lokalrezidiven und Metastasen

	Oxford		
	LoE	GR	AGO
<u>Therapie des Lokalrezidivs:</u>			
▪ R0-Resektion	4	C	++
▪ Adjuvante Radiotherapie bei Hochrisiko (Größe > 5 cm, R1)	4	C	+/-
<u>Fernmetastasierung / nicht resektable Tumoren:</u>			
▪ Therapie wie Weichteilsarkome	4	C	++
▪ Paclitaxel weekly / liposomales Doxorubicin (bei Angiosarkomen)	2b	B	+
▪ Antiangiogene Therapie (z.B. bei Angiosarkom)	4	C	+/-

Treatment of local recurrences


1. Lahat, G., Dhuka, A. R., Lahat, S., et al. (2009). Outcome of Locally Recurrent and Metastatic Angiosarcoma. *Annals of Surgical Oncology*, 16(9), 2502–2509. <http://doi.org/10.1245/s10434-009-0569-3>
2. Seinen, J. M., Styring, E., Verstappen, V., et al. (2012). Radiation-associated angiosarcoma after breast cancer: high recurrence rate and poor survival despite surgical treatment with R0 resection. *Annals of Surgical Oncology*, 19(8), 2700–2706. <http://doi.org/10.1245/s10434-012-2310-x>

Treatment of metastatic and non-resectable tumors

1. Lindner, L. H., Angele, M., Dürr, H. R., et al. (2014). Systemische Therapie und Hyperthermie beim lokal fortgeschrittenen Weichteilsarkom. *Chirurg*, 85(5), 398–403. <http://doi.org/10.1007/s00104-013-2687-5>
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from first recurrence of secondary breast angiosarcoma. *Tumori*, 95(6), 828–831.

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Brust-Implantat-assoziiertes großzellig-anaplastisches Lymphom (BIA-ALCL)

- **Selten, 3% aller Non-Hodgkin-Lymphome, 0,04–0,5% aller malignen Brusterkrankungen**
- **geschätzte jährliche Inzidenz 0,6–1,2 je 100,000 Frauen mit Implantaten (medianes Patientenalter 54 J.)**
- **Auftreten überwiegend bei texturierten Implantaten**
- **5-Jahres-OAS 89%**
- **Intervall zur Lymphomdiagnose: 8 Jahre (Median)**
- **Klinische Präsentation**
 - Schwellung und Serom (60%)
 - Tumoröse Raumforderung (17%)
 - Serom und Raumforderung (20%)
- **Histologisch: CD30+ / ALK-T-Zell-Lymphom**
- **Meldepflicht als SAE nach § 3 MPSV an das BfArM**


Reviews

1. Kim, B., Predmore, Z. S., Mattke, S., et al. (2015). Breast Implant-associated Anaplastic Large Cell Lymphoma: Updated Results from a Structured Expert Consultation Process. Plastic and Reconstructive Surgery. Global Open, 3(1), e296. <http://doi.org/10.1097/GOX.0000000000000268>
2. Eaves, F., & Nahai, F. (2011). Anaplastic large cell lymphoma and breast implants: FDA report. Aesthetic Surgery Journal, 31(4), 467–468. <http://doi.org/10.1177/1090820X11407872>
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			Oxford	
			LoE	GR AGO
	▪ Sonographie (Abklärung neu aufgetretener Serome 1 Jahr nach Implantateinlage, Herdbefund)		5	D ++
	▪ Mamma-MRT bei Bestätigung der Diagnose		5	D ++
	▪ Nodalstatus, PET-CT, Knochenmarksbiopsie		5	D ++
	▪ Ergusszytologie (bei neu aufgetretenen Seromen 1 Jahr nach Implantateinlage) mit Fragestellung „Z.A. BIA-ALCL“		5	D ++
	▪ Lymphomdiagnostik am Resektat und histologisches Staging (n. Clemens 2016)		5	D ++
	▪ Dokumentation des Implantates (Hersteller, Größe, Füllung, Oberfläche, Batch-Nummer)		5	D ++

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			Oxford	
			LoE	GR AGO
	■ Implantatentfernung und vollständige Capsulektomie einschließlich Tumorentfernung		3a	C ++
	■ Entfernung suspekter Lymphknoten, keine routinemäßige Sentinel-Node Biospie, keine Axilladisektion		4	D ++
	■ Polychemotherapie (z.B. CHOP) bei extrakapsulärer Tumorausbreitung		4	D +
	■ Radiatio bei unresektablen Tumoren oder R1		5	D +/-
	■ Rekonstruktion nach 1 Jahr erscheinungsfreiem Intervall		5	D +

1. Clemens, M. W., Medeiros, L. J., Butler, C. E., et al. (2016). Complete Surgical Excision Is Essential for the Management of Patients With Breast Implant-Associated Anaplastic Large-Cell Lymphoma. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology*, 34(2), 160–168. <http://doi.org/10.1200/JCO.2015.63.3412>
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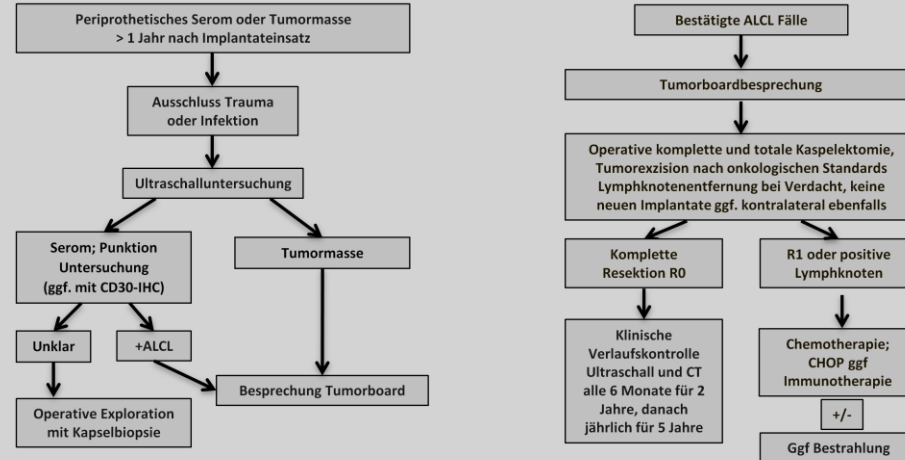
Management Implantatrekonstruktion

- **Risikoaufklärung für ein BIA-ALCL vor Implantateinlagen**
- **Halbjährliche klinische Untersuchung in den ersten 5 Jahren**
- **Ultraschalluntersuchung in den ersten 2 Jahren**
- **Bei allen spät auftretenden Seromen und reseziertem Kapselgewebe Ausschluss einer ALCL**

Blohmer, J.-U., Sinn, H.P., (2017). 243rd Statement by the German Society of Gynecology and Obstetrics (DGGG) in Response to the call for Data on the Safety of PIP Silicone Breast Implants and the Possible Association between Breast Implants and ALCL by the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) of the European Commission. Geburtshilfe Frauenheilkd, 77(06):617, doi:10.1055/s-0043-106280.

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Brust-Implantat-assoziiertes großzellig-anaplastisches Lymphom (BIA-ALCL) – Schemata zum Management (n. Noah 2017) –



Metaplastisches Mammakarzinom			
	Oxford		
	LoE	GR	AGO
■ Bildgebung und Histologie zur Diagnosesicherung nach üblichem Standard	5	D	++
■ Staging mittels CT-Thorax/ -Abdomen (hämatogene Metastasierung)	4	C	++
■ Operative Therapie nach den üblichen Grundsätzen (häufiger MRM aufgrund fortgeschrittenen Tumorstadiums)	4	C	++
■ SNB	4	C	+
■ Adjuvante Chemotherapie (eher chemoresistent)	4	C	+
■ Adjuvante endokrine Therapie nach Standard	4	C	+/-
■ Adjuvante Strahlentherapie nach Standard	4	C	+



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Imaging, Prognosis, Staging

1. Lakhani SR, Ellis IO, Schnitt SJ, et al. WHO classification of tumors of the breast. World Health Organization classification of tumours. 4th ed. Lyon: IARC Press; 2012. 48–52 pp.
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4. Sinn HP, Kreipe H. A brief overview of the WHO classification of breast tumors, 4th edition, focusing on issues and updates from the 3rd edition. Breast Care (Basel) 2013; 8:149-54.

Therapy review:

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Adjuvant endocrine therapy

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Adjuvant radiotherapy

1. Tseng WH, Martinez SR. Metaplastic breast cancer: to radiate or not to radiate? Ann Surg Oncol 2011; 18:94-103.



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Metaplastisches Mammakarzinom

Häufigkeit: 0,2-5 % aller Mammakarzinome (1)

Histologie: epitheliale und mesenchymale Anteile mit zwei bis drei unterschiedlichen Komponenten innerhalb eines Tumors; hohe Proliferationsrate Subtypen: nach WHO (4)

Metaplastic carcinoma of no special type	Low-grade adenosquamous carcinoma
Fibromatosis-like carcinoma	Squamous cell carcinoma
Spindle cell carcinoma	Metaplastic carcinoma with mesenchymal differentiation
Chondroid differentiation	Osseous differentiation
Other types of mesenchymal differentiation	Mixed metaplastic carcinoma
Myoepithelial carcinoma	

Molekularbiologie: > 90 % ER-, PR-, HER2-
in ca. 70 % Überexpression von HER1, CK 5/6-Expression
(stem-cell-like and BRCA-like)(2)
molekulares Profil hauptsächlich basal-like (3)
häufige Mutationen in PIK3CA und PTEN (mTOR-Überaktivität)

Klinik:

- große Tumore bei Erstmanifestation (> 5 cm)
- hohes hämatogenes Metastasierungspotenzial; Nodalbefall in ca. 20 % (kein Nodalbefall bei spindelförmigem Subtyp und Karzinosarkom)
- klinischer Verlauf ungünstiger als TNBC
- prognostisch ungünstiger bei asiatischen Patientinnen (häufiger MRM, schlechtes Grading, häufig plattenepithelialer Subtyp, seltener spindelförmig)

Metaplastic breast cancer - Background

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