Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Guidelines Breast
Version 2025.1E

FORSCHEN
LEHREN
HEILEN

Breast Cancer:
Specific Situations

Screened data bases:
Pubmed 2007 - 2024, ASCO 2010 – 2024, SABCS 2010 – 2024, Cochrane Data Base (2024)

Screened Guidelines:

1. Paluch-Shimon S, Cardoso F, Partridge AH, et al. ESO-ESMO fifth international consensus guidelines for breast cancer in young women (BCY5). Ann Oncol 2022;33:1097–1118.
2. Cardoso F, Paluch-Shimon S, Senkus E, et al. 5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5). Ann Oncol. 2020;31(12):1623-1649. doi:10.1016/j.annonc.2020.09.010
3. https://www.esmo.org/guidelines/breast-cancer
4. ASCO (American Association of Clinical Oncology, Practice Guidelines) http://www.asco.org
5. CMA (Canadian Medical Association): http://www.cmaj.ca
6. NCCN (National Comprehensive Cancer Network) vs. 6/2024: http://www.nccn.org
7. https://www.awmf.org/uploads/tx_szleitlinien/032-045OLk_S3_Mammakarzinom_2021-07_1.pdf

Guidelines Breast
Version 2025.1E

Breast Cancer:
Specific Situations

- **Versions 2005–2024:**
  Dall / Ditsch / Fehm / Fersis / Friedrich / Gerber / Gluz / Göhring / Harbeck / Huober / Janni / Kolberg-Liedtke / Loibl / Lück / Lux / Maass / Mundhenke / Müller / Oberhoff / Rody / Scharl / Schmidt / Schneeweiss / Schütz / Sinn / Solomayer / Stickeler / Thomssen

- **Version 2025:**
  Ditsch / Fehm

Guidelines Breast
Version 2025.1E

Content – Specific Situations

- **Frail, elderly patients**
  - **Geriatric assessment**
- **Male patients**
- **Inflammatory breast cancer (IBC, cT4d)**
- **Axillary metastases in occult breast cancer (ax. CUP)**
- **Paget's disease**
- **Malignant and Boderline Phylloides-Tumor**
- **Sarcoma, Angiosarcoma**
- **Metaplastisc breast cancer**

Treatment for Elderly Patients

AGO ++

- In general, treatment recommendations are the same as for ~~the~~ "younger patients", taking into account different biological, physical, psychological and treatment-related factors and the geriatric assessment (GA).
- Treatment options and recommendations are based on an assessment of the patient's physical condition, vulnerability, frailty, life expectancy and individual goals, and not just on age.
- It is integrated into a collaborative decision-making process, taking into account the values and goals of the individual patient.

1. Biganzoli L, et al: Updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG) .Review Lancet Oncol. 2021 Jul;22(7):e327-e340. doi: 10.1016/S1470-2045(20)30741-5. Epub 2021 May 14.
2. Carmona-Gonzalez Ca, et al: Current approaches to the pharmacological management of metastatic breast cancer in older women. Review. Pages 1785-1794 | Received 22 Apr 2024, Accepted 04 Sep 2024, Published online: 16 Sep 2024
3. Shi J, et al.: Fraility status among the elderly of different genders and the death risk. A follow-up study. Front. Med., 13 August 2021. Sec. Geriatric Medicine Volume 8 - 2021 | https://doi.org/10.3389/fmed.2021.715659
4. Lorentsen MK, Vohra S, Muss HB, et al.: Age and competing concerns in treatment selection for women with non-metastatic HR+ and HER2- breast cancer: Current clinical practice. J Geriatr Oncol 2022;13:839–843.
5. 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.
6. Minami CA, et al: Trends in Locoregional Therapy in Older Women with Early-Stage Hormone Receptor-Positive Breast Cancer by Frailty and Life Expectancy. Ann Surg Oncol 2024 Feb;31(2):920-930. doi: 10.1245/s10434-023-14446-8. Epub 2023 Oct 18.
7. Wyld L, et al: Improving outcomes for women aged 70 years or above with early breast cancer: research programme including a cluster RCT.Programme Grants for Applied Research, No. 10.6. National Institute for Health and Care Research; 2022 Jun.
8. Eochagain CM: Reporting of older subgroups in registration breast cancer trials 2012-2021. Breast Cancer Res Treat. 2023

Dec;202(3):411-421.doi: 10.1007/s10549-023-07081-0. Epub 2023 Sep 4.

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. Yood MU: Mortality impact of less-than-standard therapy in older breast cancer patients.J Am Coll Surg. 2008 Jan;206(1):66-75
9. 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. 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.
3. 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.
4. 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
5. 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.
6. 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.
7. Hills RK, et al (EBCTCG).: Immediate breast surgery versus deferral of any surgery in women aged 70+ years with operable breast cancer: patient-level meta-analysis of the three randomised trials among 1,082 patients. SABCS, 2024
8. Daly GR, et al: Impact of Sentinel Lymph Node Biopsy on Management of Older Women With Clinically Node-Negative, Early-Stage, ER+/HER2-, Invasive Breast Cancer: A Systematic Review and Meta-Analysis. Clin Breast Cancer 2024 Dec;24(8):e681-e688.e1. doi: 10.1016/j.clbc.2024.07.012. Epub 2024 Aug 8.
9. Reimer T., et al: Axillary Surgery in Breast Cancer — Primary Results of the INSEMA Trial. DOI: 10.1056/NEJMoa2412063

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. 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
3. 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
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(9472):1687-717

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. Du XL: 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
4. Muss HB et al., Adjuvant chemotherapy in older and younger women with lymph node-positive breast cancer. JAMA 2005,

293:1073-81.
5. Hurria A et al., Patterns of toxicity in older patients with breast cancer receiving adjuvant chemotherapy. Breast Cancer Res Treat. 2005 92:151-6.
6. Brunello A et al., Adjuvant chemotherapy for elderly patients (> or =70 years) with early high-risk breast cancer: a retrospective analysis of 260 patients. Ann Oncol. 2005 16:1276-82.

Statement: Chemotherapy in pts. > 70 years

1. Battisti NML, Glas N de, Soto-Perez-de-Celis E, et al.: Chemotherapy and gene expression profiling in older early luminal breast cancer patients: An International Society of Geriatric Oncology systematic review. Eur J Cancer 2022;172:158–170
2. Brain E, Viansone AA, Bourbouloux E, et al. Final results from a phase III randomized clinical trial of adjuvant endocrine therapy ± chemotherapy in women ≥ 70 years old with ER+ HER2- breast cancer and a high genomic grade index: The Unicancer ASTER 70s trial. JCO. 2022;40(16_suppl):500. doi:10.1200/JCO.2022.40.16_suppl.500.
3. 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.
4. von Minckwitz G, Reimer T, Potenberg J, et al. The phase III ICE study: Adjuvant Ibandronate with or without capecitabine in elderly patients with moderate or high risk early breast cancer. SABCS 2014 (S3-04).
5. Loibl S. et al Present Status of Adjuvant Chemotherapy for Elderly Breast Cancer Patients Breast Care 2012:7:439-444
6. Muss HB, Adjuvant chemotherapy in older women with early-stage breast cancer.N Engl J Med. 2009 May 14;360(20):2055-65.
7. 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
8. Muss HB: Adjuvant treatment of elderly breast cancer patients. Breast. 2007 Nov;16 Suppl 2:159-65
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.
10. Tamirisa N, Lin H, Shen Y, et al. Association of Chemotherapy With Survival in Elderly Patients With Multiple Comorbidities and Estrogen Receptor-Positive, Node-Positive Breast Cancer. JAMA Oncol 2020;6:1548-54.
11. Pu S, et al: Evaluation of outcome of chemotherapy for breast cancer patients older than 70 years: A SEER-based study. 2023 Mar 28:13:992573. doi: 10.3389/fonc.2023.992573. eCollection 2023.

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
5. Hughes KS et al: Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. J Clin Oncol. 2013;31(19):2382-7
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: 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
3. 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
4. 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
5. Adamo V et al. The Risk of Toxicities from Trastuzumab, Alone or in Combination, in an Elderly Breast Cancer Population. Oncology 2013;86(1):16-21.
6. Albanell J et al. Trastuzumab in small tumours and in elderly women. Cancer Treat Rev. 2014;40(1):41-7.
7. 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
8. Wilbers A, et al: Systemic Therapy in Elderly Patients With Her2/Neu-Positive Breast Cancer: A SEER Database Study.Am Surg. 2023 Dec;89(12):5690-5696. doi: 10.1177/00031348231173993. Epub 2023 May 3.

Treatment for Frail Patients

(Life Expectancy < 5 yrs., Substantial Comorbidities)

	Oxford LoE	Oxford GR	AGO
Reduced standard treatment	**2b**	**C**	**++**
Options extrapolated from trials in elderly:			
No breast surgery to prolong life (consider endocrine therapy)	2b	C	+
Breast surgery for local control	1a[a]	A	+
No axillary clearing for cN0	2b	B	+
Endocrine therapy (HR+)	1a	A	+
Endocrine therapy alone (without surgery/radiotherapy at first diagnosis)	2b	B	+
No endocrine adj. therapy after BCS and radiotherapy	1b	A	+
No radiotherapy for pT1, pN0, R0, ER / PR positive, HER2-negative, endocrine adj. therapy	1a	B	+
No radiotherapy for pT2-3, ER /PR positive, HER2- negative, endocrine adj. therapy	2b	B	+/-

1. Walzer DE Measuring the value of radiotherapy in older women with breast cancer J Clin Oncol 2012 30 (23) 2809-2811
2. Audisio RA et al When reporting on older patients with cancer , frailty information is needed Ann Surg Oncol 2011; 18: 4-5
3. Smith BD et al Improvement in breast cancer outcomes over time: are older missing out? J Clin Oncol 2011 29 (35) 4647-4653
4. Hughes KS et al Lumpectomy plus tamoxifen with or without irradiation in women age 70 or older with early breast cancer 2010 J Clin Oncol 28:69s (suppl 15, abstr 507).

Statement: Reduced standard treatment

Statement: No breast surgery (consider endocrine options)

1. Hind D: Surgery versus primary endocrine therapy for operable primary breast cancer in elderly women (70 years plus). Cochrane Database Syst Rev. 2006 Jan 25;(1):CD004272.
2. Fentiman IS, et al. 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) 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.
4. 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.
5. Hamaker ME et al. Omission of surgery in elderly patients with early stage breast cancer. Eur J Cancer 2013;49(3):545-52.
6. 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
3. Reimer T., et al: Axillary Surgery in Breast Cancer — Primary Results of the INSEMA Trial. DOI: 10.1056/NEJMoa2412063
4. Castelo M, et al: The Association Between Surgical Axillary Staging, Adjuvant Treatment Use and Survival in Older Women with Early Stage Breast Cancer: A Population-Based Study. Ann Surg Oncol 2023 Jul;30(7):3901-3912. doi: 10.1245/s10434-023-13274-0. Epub 2023 Mar 14.

Statement: No radiotherapy (≥ 70 y, pT1, pN0, ER+)

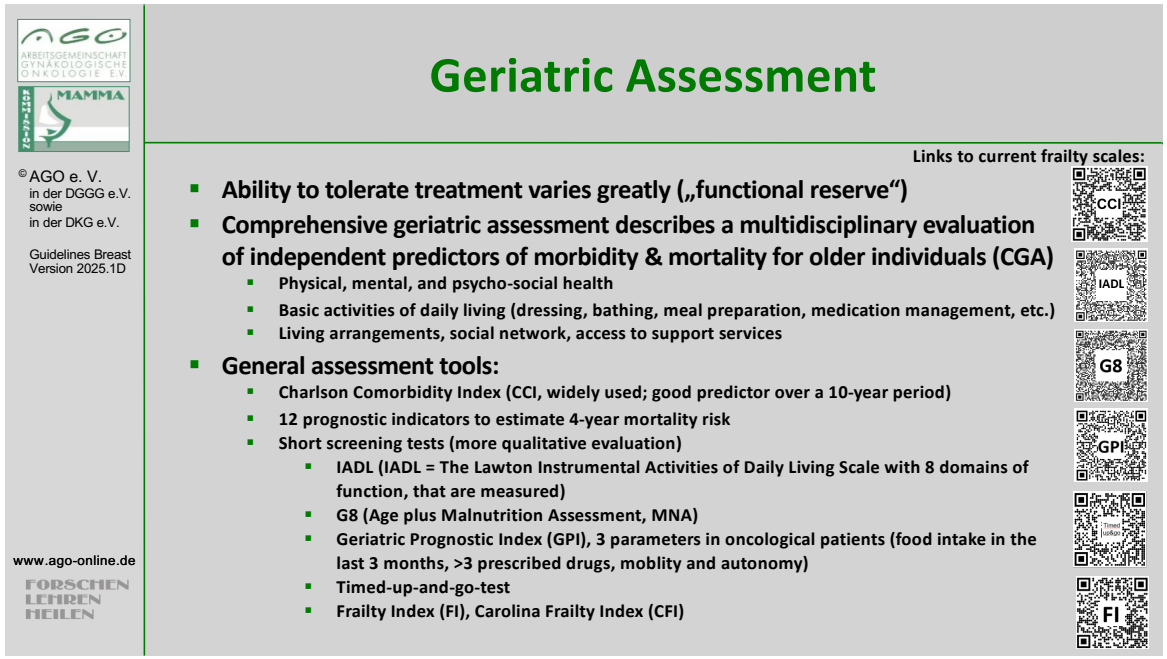
1. Kim YJ, Shin KH, Kim K. Omitting Adjuvant Radiotherapy for Hormone ReceptorPositive Early-Stage Breast Cancer in Old Age: A Propensity Score Matched SEER Analysis. Cancer research and treatment : official journal of Korean Cancer Association 2018.
2. Hannoun-Levi JM, et al. Breast cancer in elderly women: is partial breast irradiation a good alternative? Breast Cancer Res Treat. 2003 Oct;81(3):243-51
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. 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
5. 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.
6. Stueber TN, Diessner J, Bartmann C, et al. Effect of adjuvant radiotherapy in elderly patients with breast cancer. PLOS ONE 2020;15:e0229518.

Statement: Hypofractionated radiotherapy

1. 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.
2. Veronesi U, Orecchia R, Maisonneuve P, et al. Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial. Lancet Oncol. 2013 Dec;14(13):1269-77.
3. 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.
4. 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
5. Haussmann J, Budach W, et al: Whole Breast Irradiation in Comparison to Endocrine Therapy in Early Stage Breast Cancer—A Direct and Network Meta-Analysis of Published Randomized Trials. Cancers 2023, 15, 4343. https:// doi.org/10.3390/cancers15174343

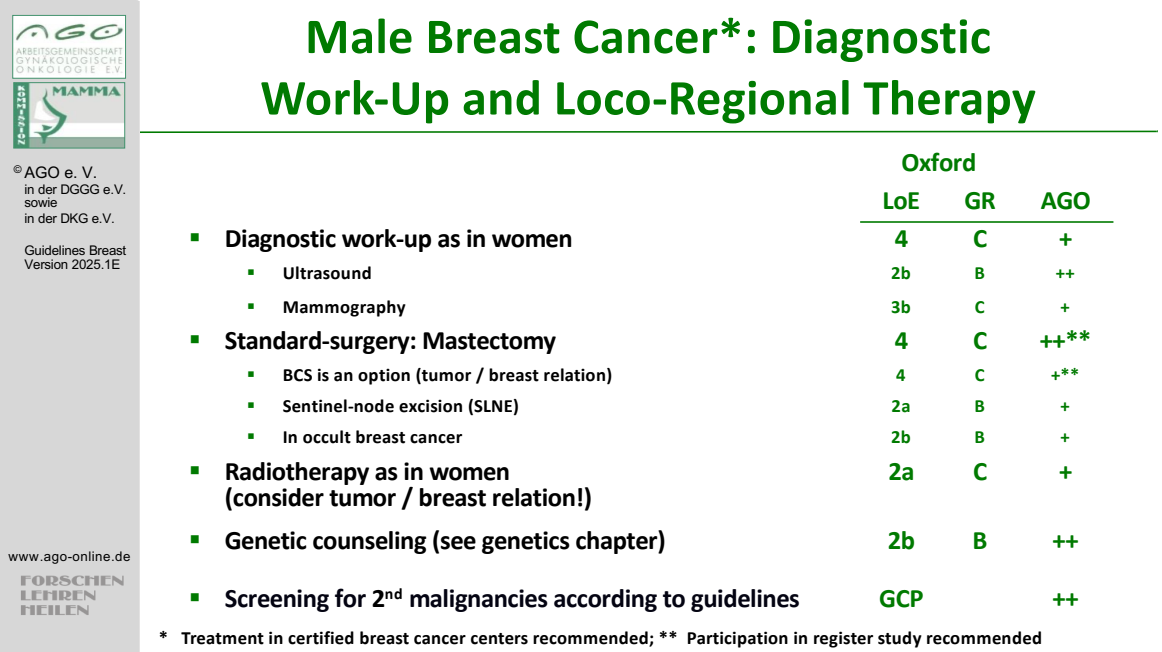
Statement: No chemotherapy > 70 years and negative risk benefit analysis

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.



1. Jung C, Bruno RR, Wernly B et al. Frailty as a Prognostic Indicator in Intensive Care. Dtsch Arztebl Int. 2020 Oct 2;117(40):668-673.
2. van Walree IC, Scheepers E, van Huis-Tanja L et al. A systematic review on the association of the G8 with geriatric assessment, prognosis and course of treatment in older patients with cancer. J Geriatr Oncol. 2019 Nov;10(6):847-858.
3. Williams GR, Deal AM, Sanoff HK et al. Frailty and health-related quality of life in older women with breast cancer. Support Care Cancer. 2019 Jul;27(7):2693-2698.
4. 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.
5. van Abbema D, van Vuuren A, van den Berkmortel F et al. Functional status decline in older patients with breast and colorectal cancer after cancer treatment: A prospective cohort study. J Geriatr Oncol. 2017 May;8(3):176-184.
6. Martinez-Tapia C, Canoui-Poitrine F, Bastuji-Garin S et al. Optimizing the G8 Screening Tool for Older Patients With Cancer: Diagnostic Performance and Validation of a Six-Item Version. Oncologist. 2016 Feb;21(2):188-95.
7. 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.
8. 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.
9. Aaldriks AA. Prognostic value of geriatric assessment in older patients with advanced breast cancer receiving chemotherapy et al.

Breast 2013;22(5):753-60.
10. Bellera CA et al. Screening older cancer patients: first evaluation of the G-8 geriatric screening tool. Ann Oncol. 2012;23(8):2166-72
11. Hamaker ME, Jonker JM, de Rooij SE et al. Frailty screening methods for predicting outcome of a comprehensive geriatric assessment in elderly patients with cancer: a systematic review. Lancet Oncol. 2012 Oct;13(10):e437-44.
12. 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.
13. Farhat JS, Velanovich V, Falvo AJ et al. Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. J Trauma Acute Care Surg. 2012 Jun;72(6):1526-30; discussion 1530-1.
14. Lee et al. Development and validation of a prognostic index for 4-year mortality in older adults. JAMA 2006 295:801-08.
15. Guigoz Y, Vellas B, Garry PJ. Assessing the nutritional status of the elderly: The Mini Nutritional Assessment as part of the geriatric evaluation. Nutr Rev. 1996 Jan;54(1 Pt 2):S59-65.
16. Charlson et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis 1987 40:373-383.
17. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist. 1969 Autumn;9(3):179-86.



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.
2. Doebar SC, Slaets L, Cardoso F et al. Male breast cancer precursor lesions: analysis of the EORTC 10085/TBCRC/BIG/NABCG International Male Breast Cancer Program. Mod Pathol 2017;30(4):509-18.
3. Vermeulen MA, Slaets L, Cardoso F et al. Pathological characterisation of male breast cancer: Results of the EORTC 10085/TBCRC/BIG/NABCG International Male Breast Cancer Program. Eur J Cancer 2017;82:219-27.

General

1. Gucalp A, Traina TA, Eisner JR, 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, 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, et al. Male breast cancer: a disease distinct from female breast cancer. Breast Cancer Res Treat 2018.

9. Wang K, Wang QJ, Xiong YF, et al. Survival Comparisons Between Early Male and Female Breast Cancer Patients. Scientific reports 2018;8(1):8900.
10. Heinig J: Clinical management of breast cancer in males: a report of four cases. Eur J Obstet Gynecol Reprod Biol. 2002 Apr 10;102(1):67-73
11. Thalib L ,Hall P. Survival of male breast cancer patients: Population-based cohort study. Cancer Sci. 2008
12. 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.
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. Kuo SH et al. Comprehensive locoregional treatment and systemic therapy for postmastectomy isolated locoregional recurrence, Int J Radiat Oncol Biol Phys. 2008 Dec 1;72(5):1456-64. Epub 2008 Aug 7

4. 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.
5. Fields EC et al. Management of male breast cancer in the United States: a surveillance, epidemiology and end results analysis. J Radiat Oncol Biol Phys 2013;87(4):747-52
6. Cloyd et al. Outcomes of partial mastectomy in male breast cancer patients: analysis of SEER, 1983-2009. Ann Surg Oncol. 2013;20:1545–50
7. 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.
8. Wong WG, Perez Holguin RA, Kanwar R, et al. Management of Male Patients With Occult Breast Cancer: Analysis of the National Cancer Database. J Surg Res 2024; 293: 685-692

Statement: Surgery: BEO – men

1. Cloyd JM, Hernandez-Boussard T, Wapnir IL. Outcomes of partial mastectomy in male breast cancer patients: analysis of SEER, 1983–2009. Ann Surg Oncol. 2013;20(5):1545–50.
2. Bratman SV, Kapp DS, Horst KC. Evolving trends in the initial locoregional management of male breast cancer. Breast. 2012;21(3):296–302. https://doi.org/10.1016/j.breast.2012.01.008.
3. Golshan M, Rusby J, Dominguez F, et al. Breast conservation for male breast carcinoma. Breast. 2007;16(6):653–6.
4. Serarslan A, Gursel B, Okumus NO, et al. Male breast cancer: 20 years experience of a tertiary hospital from the Middle Black Sea Region of Turkey. Asian Pac J Cancer Prev. 2015;16(15):6673–9.

Statement: Sentinel-node excision (SNE)

1. 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
2. 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
3. Parpex G, et al: Accuracy of sentinel lymph node biopsy in male breast cancer: Systematic review and meta-analysis.,Breast. 2024 Mar 5;75:103703. doi: 10.1016/j.breast.2024.103703

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

1. Eggemann H et al. Male breast cancer: 20-year survival data for post-mastectomy radiotherapy. Breast Care (Basel). 2013;8(4):270-5.
2. Colciago RR, et al: The role of radiation therapy in the multidisciplinary management of male breast cancer: A systematic review and meta-analysis on behalf of the Clinical Oncology Breast Cancer Group (COBCG). Crit Rev Oncol Hematol. 2024 Dec:204:104537. doi: 10.1016/j.critrevonc.2024.104537. Epub 2024 Oct 23.

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

1. Pellini F, Granuzzo E, Urbani S et al. Male Breast Cancer: Surgical and Genetic Features and a Multidisciplinary Management Strategy. Breast Care (Basel). 2020 Feb;15(1):14-20.

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. 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. 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. 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
2. Agrawal A, Ayantunde AA, Rampaul R et al. Male breast cancer: a review of clinical management. Breast Cancer Res Treat. 2006 Oct 11;
3. Korde LA et al: Multidisciplinary meeting on male breast cancer; summary and research recommendations J Clin Oncol 28: 2114-2122, 2010

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

Male Breast Cancer: Prognostic Factors

	Oxford		
	LoE	GR	AGO
▪ Nodal status	2b	A	++
▪ Age	2b	B	+
▪ Tumor size	2b	A	++
▪ ER / PR Expression	2b	A	++
▪ Ki-67 Expression	2b	C	+/-
▪ Grade	2b	C	+/-
▪ Genomic signatures	2b	B	+

Registries

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.
2. Doebar SC, Slaets L, Cardoso F et al. Male breast cancer precursor lesions: analysis of the EORTC 10085/TBCRC/BIG/NABCG International Male Breast Cancer Program. Mod Pathol 2017;30(4):509-18.
3. Vermeulen MA, Slaets L, Cardoso F et al. Pathological characterisation of male breast cancer: Results of the EORTC 10085/TBCRC/BIG/NABCG International Male Breast Cancer Program. Eur J Cancer 2017;82:219-27.
4. Wang F, Reid S, Zheng W, et al. Sex Disparity Observed for Oncotype DX Breast Recurrence Score in Predicting Mortality Among Patients with Early Stage ER-Positive Breast Cancer. Clinical Cancer Research 2020;26:101-9.
5. Massarweh SA, Sledge GW, Miller DP, McCullough D, Petkov VI, Shak S. Molecular Characterization and Mortality From Breast Cancer in Men. Journal of Clinical Oncology 2018;36:1396-404.

Male Breast Cancer: Systemic Therapy

	Oxford		
	LoE	GR	AGO
▪ **(Neo-)adjuvant chemotherapy as in women**	2a	B	++
▪ **HER2-targeted therapy (if HER2-positive)**	5	D	++
▪ **Endocrine therapy**	4	D	++
▪ Tamoxifen	2b	B	++
▪ GnRHa and AI	4	C	+
▪ Aromatase inhibitors without GnRHa	2b	B	-
▪ Fulvestrant (metastatic BC)	4	C	+/-
▪ CDK4/6i (in combination)	2b	B	+
▪ **Palliative chemotherapy as in women**	4	C	++

Statement: Adjuvant Chemotherapy

1. Giordano SH, Perkins GH, Broglio K, et al. Adjuvant systemic therapy for male breast cancer. Cancer 2005; 104: 235-264
2. 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 CDK4/6i

1. Wedam S, Fashoyin-Aje L, Bloomquist E, et al.:FDA Approval Summary: Palbociclib for Male Patients with Metastatic Breast Cancer. Clin Cancer Res. 2019 Oct 24. doi: 10.1158/1078-0432.CCR-19-2580.

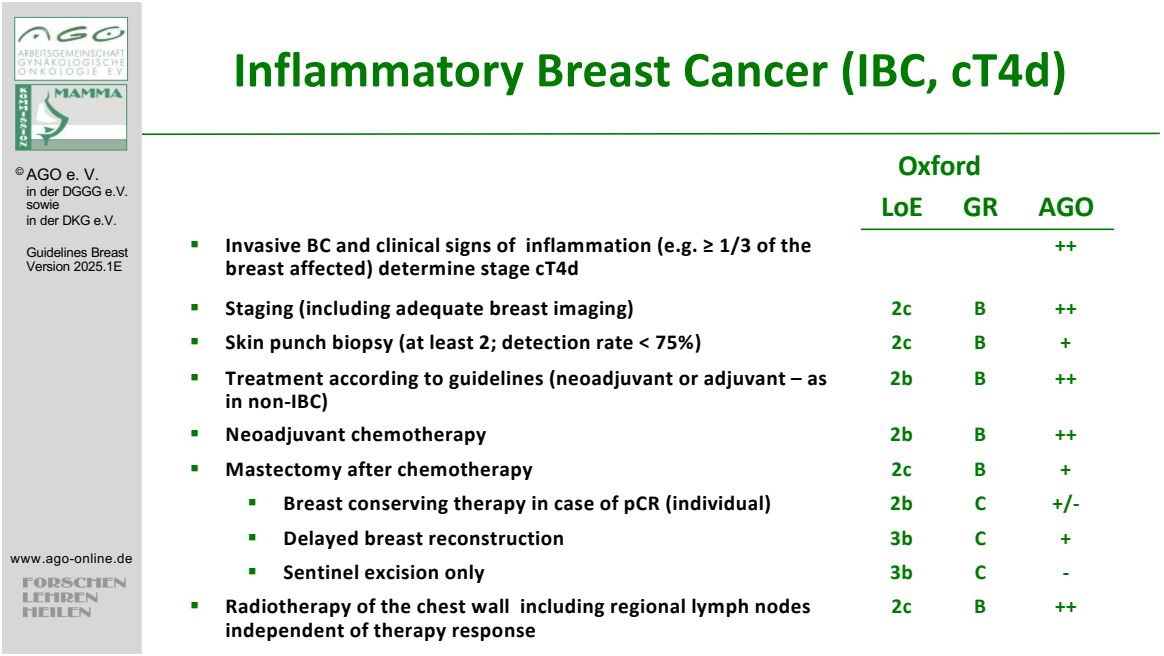
Statement endocrine therapy

1. Ribeiro G et al. Adjuvant tamoxifen for male breast cancer (MBC). Br J Cancer 1992 65: 252
2. Agrawal: Fulvestrant in advanced male breast cancer. Breast Cancer Res Treat. 2007 Jan;101(1):123. Epub 2006 Jun 29.

3. 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
4. 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
5. Giordano SH: Efficacy of anastrozole in male breast cancer. Am J Clin Oncol 2002 25: 235-237
6. Giordano SH: Leuprolide acetate plus aromatase inhibition for male breast cancer. J Clin Oncol. 2006 Jul 20;24(21):e42-3. No abstract available.
7. Arriola E: Aromatase inhibitors and male breast cancer. Clin Transl Oncol. 2007 Mar;9(3):192-4
8. 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.
9. 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
10. 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
11. Eggemann H, Brucker C, Schrauder M, et al. Survival benefit of tamoxifen in male breast cancer: prospective cohort analysis. British journal of cancer 2020;123:33-7.
12. Reinisch M, et al. Efficacy of Endocrine Therapy for the Treatment of Breast Cancer in Men: Results from the MALE Phase 2 Randomized Clinical Trial. JAMA Oncol. 2021 Apr 1;7(4):565-572.

<u>Statement palliative chemotherapy</u>

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



Inflammatory Breast Cancer (IBC, cT4d)

	Oxford LoE	Oxford GR	AGO
▪ Invasive BC and clinical signs of inflammation (e.g. ≥ 1/3 of the breast affected) determine stage cT4d			++
▪ Staging (including adequate breast imaging)	2c	B	++
▪ Skin punch biopsy (at least 2; detection rate < 75%)	2c	B	+
▪ Treatment according to guidelines (neoadjuvant or adjuvant – as in non-IBC)	2b	B	++
▪ Neoadjuvant chemotherapy	2b	B	++
▪ Mastectomy after chemotherapy	2c	B	+
▪ Breast conserving therapy in case of pCR (individual)	2b	C	+/-
▪ Delayed breast reconstruction	3b	C	+
▪ Sentinel excision only	3b	C	-
▪ Radiotherapy of the chest wall including regional lymph nodes independent of therapy response	2c	B	++

Guidelines:

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines(r)). Breast Cancer. Version 6.2024 NCCN.org (Inflammatory Breast Cancer. IBC-1)

General

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):1437-47.1
2. Audisio RA. Inflammatory Breast Cancer: Updates on diagnosis and treatment options. Eur J Surg Oncol 2018;44(8):1127.
3. 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.
4. 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.
5. Wu SG, Zhang WW, Wang J et al. Inflammatory breast cancer outcomes by breast cancer subtype: a population-based study. Future Oncol 2018.
6. 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.
7. 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.
8. 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. ≥ 1/3 of the breast affected) determine stage cT4d

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines(r)). Breast Cancer. Version 6.2024 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.

Statement: Regimens as in non-inflammatory BC

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines(r)). Breast Cancer. Version 6.2024 NCCN.org (Inflammatory Breast Cancer. IBC-1)

Statement: Neoadjuvant chemotherapy

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines(r)). Breast Cancer. Version 6.2024 NCCN.org (Inflammatory Breast Cancer. IBC-1)
2. 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.

3. 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: Mastectomy after chemotherapy

1. Chen H, Wu K, Wang M, et al: A standard mastectomy should not be the only recommended breast surgical treatment for non-metastatic inflammatory breast cancer: A large population-based study in the Surveillance, Epidemiology, and End results database 18. Breast. 2017 Oct;35:48-54.
2. Tsai CJ et al. Outcomes after multidisciplinary treatment of inflammatory breast cancer in the era of neoadjuvant HER2-directed therapy. Am J Clin Oncol 2013 [Epub ahead of print].
3. Adesoye T, Lucci A. Current Surgical Management of Inflammatory Breast Cancer. Ann Surg Oncol. 2021 Oct;28(10):5461-5467. doi: 10.1245/s10434-021-10522-z. Epub 2021 Aug 3. PMID: 34346020.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines(r)). Breast Cancer. Version 6.2024 NCCN.org (Inflammatory Breast Cancer. IBC-1)

Statement: Immediate breast reconstruction:

1. Nakhlis F, Regan MM, Chun YS, et al. Patterns of breast reconstruction in patients diagnosed with inflammatory breast cancer: The Dana-Farber Cancer Institute's Inflammatory Breast Cancer Program experience. Breast J 2020;26(3):384–90.
2. Adesoye T, Lucci A. Current Surgical Management of Inflammatory Breast Cancer. Ann Surg Oncol. 2021 Oct;28(10):5461-5467.

Statement: Sentinel lymph node

1. Adesoye T, Lucci A. Current Surgical Management of Inflammatory Breast Cancer. Ann Surg Oncol. 2021 Oct;28(10):5461-5467. doi: 10.1245/s10434-021-10522-z..

Statement: Radiotherapy

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines(r)). Breast Cancer. Version 6.2024 NCCN.org (Inflammatory Breast Cancer. IBC-1)

Axillary Metastasis in Occult Breast Cancer (ax. CUP) Diagnostic Imaging

	Oxford		
	LoE	GR	AGO
▪ **Breast imaging incl. Breast-MRI**	3	B	++
▪ **Exclude contralateral cancer**	3	B	++
▪ **Staging** (CT thorax / abdomen, pelvis, bone scan)	3	B	++
If histological diagnosis is not certain			
▪ **Exclude non-breast malignancy, especially in case of TNBC** (e.g. NEC, female genital tract, lung, thyroid gland, stomach, skin, ENT)	5	D	++
▪ **PET / PET-CT**	3b	B	+

Statement: Mammography / Breast ultrasound/ Breast MRI

1. Schneeweiss, A. & Buschhorn, L. „Breast-like cancer of unknown primary“. Implikationen für die radiologische Diagnostik. Die Radiol. 63, 366–370 (2023)
2. Fehm, T., & Souchon, R. (2013). Axillary lymph node metastasis in CUP. Der Onkologe, 19(1), 40–43. http://doi.org/10.1007/s00761-012-2314-y
3. Foroudi, F., & Tiver, K. W. (2000). Occult breast carcinoma presenting as axillary metastases. International Journal of Radiation Oncology, Biology, Physics, 47(1), 143–147. http://doi.org/10.1007/s10147-005-0485-x
4. Ofri A, Moore K. Occult breast cancer: Where are we at? Breast. 2020 Dec;54:211-215. doi: 10.1016/j.breast.2020.10.012. Epub 2020 Oct 27.
5. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (Version3.2024).

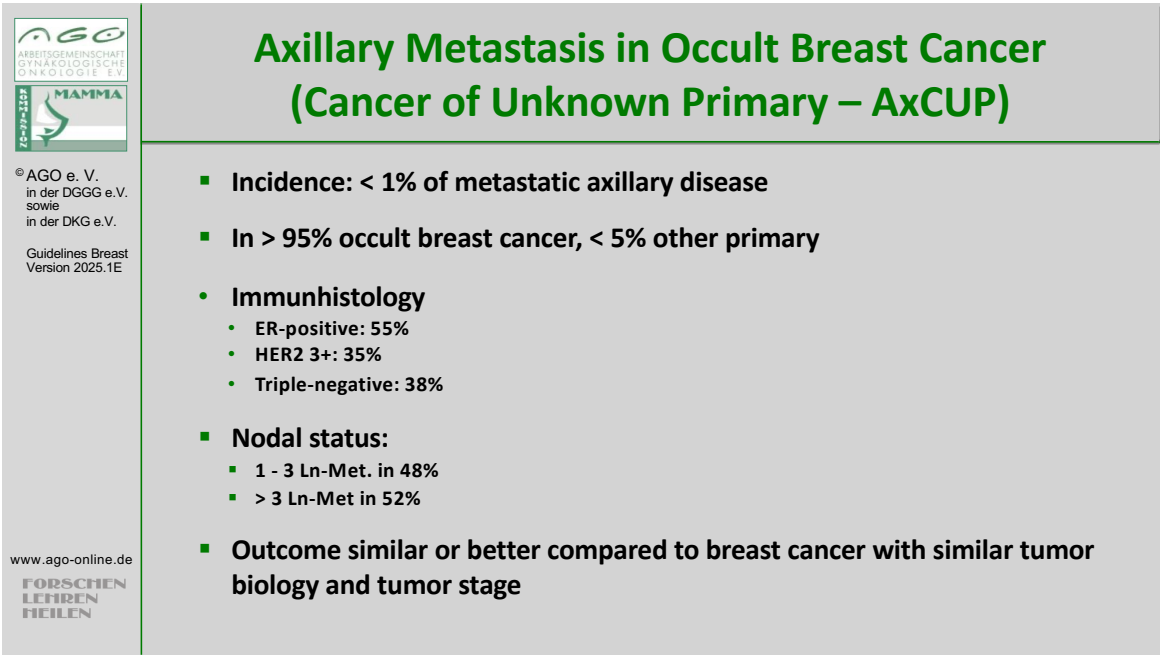
Statement: Staging

1. Steunebrink: Bilateral axillary metastases of occult breast carcinoma: report of a case with a review of the literature. Breast. 2005 Apr;14(2):165-8
2. Jerusalem, G., Rorive, A., Ancion, G. et al. (2006). Diagnostic and therapeutic management of carcinoma of unknown primary: radio-

imaging investigations. Annals of Oncology : Official Journal of the European Society for Medical Oncology / ESMO, 17 Suppl 10(suppl_10), x168–76. http://doi.org/10.1093/annonc/mdl255
3. Hemminki, K., Bevier, M., Sundquist, J., et al. (2013). Site-specific cancer deaths in cancer of unknown primary diagnosed with lymph node metastasis may reveal hidden primaries. International Journal of Cancer Journal International Du Cancer, 132(4), 944–950. http://doi.org/10.1002/ijc.27678

Statement: PET

1. Jerusalem, G., Rorive, A., Ancion, G., et al. (2006). Diagnostic and therapeutic management of carcinoma of unknown primary: radio-imaging investigations. Annals of Oncology : Official Journal of the European Society for Medical Oncology / ESMO, 17 Suppl 10(suppl_10), x168–76. http://doi.org/10.1093/annonc/mdl255
2. Kwee, T. C., & Kwee, R. M. (2009). Combined FDG-PET/CT for the detection of unknown primary tumors: systematic review and meta-analysis. European Radiology, 19(3), 731–744. http://doi.org/10.1007/s00330-008-1194-4
3. Varadhachary, G. R., Abbruzzese, J. L., & Lenzi, R. (2004). Diagnostic strategies for unknown primary cancer. Cancer, 100(9), 1776–1785. http://doi.org/10.1002/cncr.20202
4. Pelosi, E., Pennone, M., Deandreis, D., et al. (2006). Role of whole body positron emission tomography/computed tomography scan with 18F-fluorodeoxyglucose in patients with biopsy proven tumor metastases from unknown primary site. The Quarterly Journal of Nuclear Medicine and Molecular Imaging: 50(1), 15–22.



Guidelines

1. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (3.2024). Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) .
2. Krämer A. et al. Cancer of unknown primary: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up ☆. Ann Oncol 34, 228–246 (2023).
3. NICE (2010). Metastatic malignant disease of unknown primary origin in adults: diagnosis and management. Retrieved January Dec 26th, 2018, https://www.nice.org.uk/guidance/cg104/resources/metastatic-malignant-disease-of-unknown-primary-origin-diagnosis-and-management-of-metastatic-malignant-disease-of-unknown-primary-origin-35109328970437

Reviews

1. Khoury, T., Mendez, A. L. R., Peng, X., Yan, L. & Racila, E. Clinicopathologic characteristics of malignant non-hematopoietic tumors first presented as an axillary mass with emphasis on occult breast carcinoma. International Journal of Clinical Oncology 25, 292–300 (2020).
2. Pentheroudakis, G., Lazaridis, G., & Pavlidis, N. (2010). Axillary nodal metastases from carcinoma of unknown primary (CUPAx): a systematic review of published evidence. Breast Cancer Research and Treatment, 119(1), 1–11.
3. Lanitis, S., Behranwala, K. A., Al-Mufti, R., et al.(2009). Axillary metastatic disease as presentation of occult or contralateral breast

cancer. Breast (Edinburgh, Scotland), 18(4), 225–227. http://doi.org/10.1016/j.breast.2009.07.002
4. Galimberti, V., Bassani, G., Monti, S., et al. (2004). Clinical experience with axillary presentation breast cancer. Breast Cancer Research and Treatment, 88(1), 43–47. http://doi.org/10.1007/s10549-004-9453-9
5. Pentheroudakis, G., Briasoulis, E., & Pavlidis, N. (2007). Cancer of unknown primary site: missing primary or missing biology? Oncologist, 12(4), 418–425. http://doi.org/10.1634/theoncologist.12-4-418

Pathology
1. Montagna, E., Bagnardi, V., Rotmensz, et al. (2011). Immunohistochemically defined subtypes and outcome in occult breast carcinoma with axillary presentation. Breast Cancer Research and Treatment, 129(3), 867–875. http://doi.org/10.1007/s10549-011-1697-6

Outcome
1. Ouldamer L, Cayrol M, Vital M et al. Axillary lymph node metastases from unknown primary: A French multicentre study. Eur J Obstet Gynecol Reprod Biol 2018;223:103-07.
2. McCartan DP, Zabor EC, Morrow M et al. Oncologic Outcomes After Treatment for MRI Occult Breast Cancer (pT0N+). Ann Surg Oncol 2017;24(11):3141-47
3. Ge LP, Liu XY, Xiao Y et al. Clinicopathological characteristics and treatment outcomes of occult breast cancer: a SEER population-based study. Cancer Manag Res 2018;10:4381-91.
4. Sohn, G., Son, B. H., Lee, S. J., et al. (2014). Treatment and survival of patients with occult breast cancer with axillary lymph node metastasis: a nationwide retrospective study. Journal of Surgical Oncology, 110(3), 270–274. http://doi.org/10.1002/jso.23644
5. Huang KY, Zhang J, Fu WF, et al. Different Clinicopathological Characteristics and Prognostic Factors for Occult and Non-occult Breast Cancer: Analysis of the SEER Database. Front Oncol. 2020 Aug 19;10:1420. doi: 10.3389/fonc.2020.01420.

Axillary Metastasis in Occult Breast Cancer (ax. CUP)

Pathology, Molecular Pathology

	Oxford LoE	Oxford GR	Oxford AGO
▪ **Immunohistochemistry (ER, PR, HER2, Ki-67, GATA)**	5	D	++
▪ **Immunohistochemistry (e.g. Ck5/6, Ck7, Ck20, SOX-10, PAX-8, TTF1, Synaptophysin etc.) to exclude other primary malignancies in case of TNBC phenotype or unusual histology, e.g. NEC, female genital tract, lung, ENT tumors, thyroid, stomach, skin**	5	D	++
▪ **Gene expression profiling for determination or primary site (e.g. CUPprint, Pathwork, TOT, CancerType)**	2c	B	+/-
▪ **NGS, epigenetics for determination of primary site (Panel-Sequencing, e.g. EPICup)**	2c	B	+/-
▪ **Prognostic gene expression tests**	5	D	--

Immunohistochemistry

1. Santos MTD, Souza BF, Carcano FM et al. An integrated tool for determining the primary origin site of metastatic tumours. J Clin Pathol 2018;71(7):584-93.
2. http://doi.org/10.1016/j.humpath.2012.09.005
3. Montagna, E., Bagnardi, V., Rotmensz, N. et al. (2011). Immunohistochemically defined subtypes and outcome in occult breast carcinoma with axillary presentation. Breast Cancer Research and Treatment, 129(3), 867–875. http://doi.org/10.1007/s10549-011-1697-6
4. Munding, J., & Tannapfel, A. (2012). Pathology of CUP syndrome. *Der Onkologe*, *19*(1), 15–21. http://doi.org/10.1007/s00761-012-2313-z
5. Oien, K. A. (2009). Pathologic evaluation of unknown primary cancer. Seminars in Oncology, 36(1), 8–37. http://doi.org/10.1053/j.seminoncol.2008.10.009
6. Ordonez, N. G. (2013). Value of GATA3 immunostaining in tumor diagnosis: a review. Advances in Anatomic Pathology, 20(5), 352–360. http://doi.org/10.1097/PAP.0b013e3182a28a68
7. Provenzano, E., Byrne, D. J., Russell, P. A., et al(2015). Differential expression of immunohistochemical markers in primary lung and breast cancers enriched for triple-negative tumours. Histopathology, 68(3), 367–377. http://doi.org/10.1111/his.12765
8. Wang, J., Talmon, G., Hankins, J. H., et al. (2012). Occult breast cancer presenting as metastatic adenocarcinoma of unknown

primary: clinical presentation, immunohistochemistry, and molecular analysis. Case Reports in Oncology, 5(1), 9–16. http://doi.org/10.1159/000335449
9. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Occult Primary (Cancer of Unknown Primary [CUP]), Version 2.2025 — September 11, 2024, NCCN.org

Gene expression profiling and other molecular approaches in CUP disease

1. Ades, F., De Azambuja, E., Daugaard, G., et al. (2013). Comparison of a gene expression profiling strategy to standard clinical work-up for determination of tumour origin in cancer of unknown primary (CUP). Journal of Chemotherapy (Florence, Italy), 25(4), 239–246. http://doi.org/10.1179/1973947813Y.0000000085
2. Greco, F. A., Spigel, D. R., Yardley, D. A., et al. (2010). Molecular profiling in unknown primary cancer: accuracy of tissue of origin prediction. The Oncologist, 15(5), 500–506. http://doi.org/10.1634/theoncologist.2009-0328
3. Horlings, H. M., van Laar, R. K., Kerst, J.-M., et al. (2008). Gene expression profiling to identify the histogenetic origin of metastatic adenocarcinomas of unknown primary. Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 26(27), 4435–4441. http://doi.org/10.1200/JCO.2007.14.6969
4. Monzon, F. A., & Koen, T. J. (2010). Diagnosis of metastatic neoplasms: molecular approaches for identification of tissue of origin. Archives of Pathology & Laboratory Medicine, 134(2), 216–224. http://doi.org/10.1043/1543-2165-134.2.216
5. Moran, S., Martínez-Cardús, A., Sayols, S., & Musulén, E. (2016). Epigenetic profiling to classify cancer of unknown primary: a multicentre, retrospective analysis. The Lancet, 17(10), 1386–1395. http://doi.org/10.1016/S1470-2045(16)30297-2
6. Ross, J. S., Wang, K., Gay, L., et al. (2015). Comprehensive Genomic Profiling of Carcinoma of Unknown Primary Site: New Routes to Targeted Therapies. JAMA Oncology, 1(1), 40–49. http://doi.org/10.1001/jamaoncol.2014.216
7. Tothill, R. W., Shi, F., Paiman, L., et al. (2015). Development and validation of a gene expression tumour classifier for cancer of unknown primary. Pathology, 47(1), 7–12. http://doi.org/10.1097/PAT.0000000000000194
8. Varadhachary, G. R., Talantov, D., Raber, M. N., et al. (2008). Molecular profiling of carcinoma of unknown primary and correlation with clinical evaluation. Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 26(27), 4442–4448. http://doi.org/10.1200/JCO.2007.14.4378
9. Xu, Q., Chen, J., Ni, S., et al. (2016). Pan-cancer transcriptome analysis reveals a gene expression signature for the identification of tumor tissue origin. Modern Pathology, 29(6), 546–556. http://doi.org/10.1038/modpathol.2016.60

Axillary Metastasis in Occult Breast Cancer (ax. CUP): Therapy

	Oxford		
	LoE	GR	AGO
▪ **Axillary dissection**	3a	C	++
▪ **Targeted axillary dissection after NACT (in case of clinical complete remission**	3b	C	+/-
▪ **Irradiation of regional lymph nodes according to breast cancer guidelines (AGO)**	3b	B	+
▪ **Breast irradiation if breast MRI is negative (acc. BCT)**	2c	B	+
▪ **Mastectomy if breast MRI is negative**	3a	C	--
▪ **(Neo-)adjuvant systemic therapy according to breast cancer guidelines (AGO)**	5	D	++

Guidelines

1. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (Version3.2024).
2. Fizazi K, Greco FA, Pavlidis N et al. Cancers of unknown primary site: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015;26 Suppl 5:v133-8.

Reviews

1. Holt AC, Haji F, McCloskey S, Baker JL. De-escalation of surgery for occult breast cancer with axillary metastasis. Surgery. 2023 Aug;174(2):410-412.
2. Ofri A, Moore K. Occult breast cancer: Where are we at? Breast. 2020 Dec;54:211-215. doi: 10.1016/j.breast.2020.10.012. Epub 2020 Oct 27.

Statement: Axillary dissection

1. Pentheroudakis, G., Lazaridis, G., & Pavlidis, N. (2010). Axillary nodal metastases from carcinoma of unknown primary (CUPAx): a systematic review of published evidence. Breast Cancer Research and Treatment, 119(1), 1–11. http://doi.org/10.1007/s10549-009-0554-3
2. Schmidt, T., & Ulrich, A. (2014). [Surgical options in cancer of unknown primary (CUP)]. Der Radiologe, 54(2), 140–144.

http://doi.org/10.1007/s00117-013-2549-7
3. Botty Van den Bruele A, Lavery J, Plitas G, Pilewskie ML. Axillary Downstaging in Occult Primary Breast Cancer After Neoadjuvant Chemotherapy. Ann Surg Oncol. 2021 Feb;28(2):968-974. doi: 10.1245/s10434-020-08863-2. Epub 2020 Aug 19.

Statement TALD + RT nach NACT

1. Cohen BL, Collier AL, Kelly KN et al. Surgical Management of the Axilla in Patients with Occult Breast Cancer (cT0 N+) After Neoadjuvant Chemotherapy. Ann Surg Oncol. 2020 Jun;27(6):1830-1841.

Statement: Mastectomy without (in-)breast tumor

1. Li J, Liu G, Jia Z, Ren F, Dong D, Zhang M, Wang X, Wang Y. Occult breast cancer patients with mastectomy have better prognosis than those with breast-conserving therapy. Future Oncol. 2023 Nov;19(36):2405-2416. *(Kommentar: Ergebnis: Mastektomie besser (DFS, OS) als BCT. Retrospektiv. Widersprüchliche Daten, z.B. mit Radiotherapie schlechter (Faktor 2-5) als ohne (!))*
2. Ofri A, Moore K. Occult breast cancer: Where are we at? Breast. 2020 Dec;54:211-215. doi: 10.1016/j.breast.2020.10.012. Epub 2020 Oct 27. PMID: 33130487; PMCID: PMC7599122.
3. Tsai C, Zhao B, Chan T, Blair SL. Treatment for occult breast cancer: A propensity score analysis of the National Cancer Database. Am J Surg. 2020 Jul;220(1):153-160.
4. Macedo F.I. et al. Optimal surgical management for occult breast carcinoma: a meta-analysis. Ann Surg Oncol. 2016; 23: 1838-1844. *(Comment: Metaanalysis of 7 retrospective studies, n=241 pts)*
5. Schmidt, T., & Ulrich, A. (2014). Chirurgische Optionen bei “cancer of unknown primary” (CUP). Der Radiologe, 54(2), 140–144. http://doi.org/10.1007/s00117-013-2549-7
6. Khandelwal, A. K., & Garguilo, G. A. (2005). Therapeutic options for occult breast cancer: a survey of the American Society of Breast Surgeons and review of the literature. The American Journal of Surgery, 190(4), 609–613.
7. Pavlidis, N., Briasoulis, E., Hainsworth et al. (2003). Diagnostic and therapeutic management of cancer of an unknown primary. European Journal of Cancer (Oxford, England : 1990), 39(14), 1990–2005.

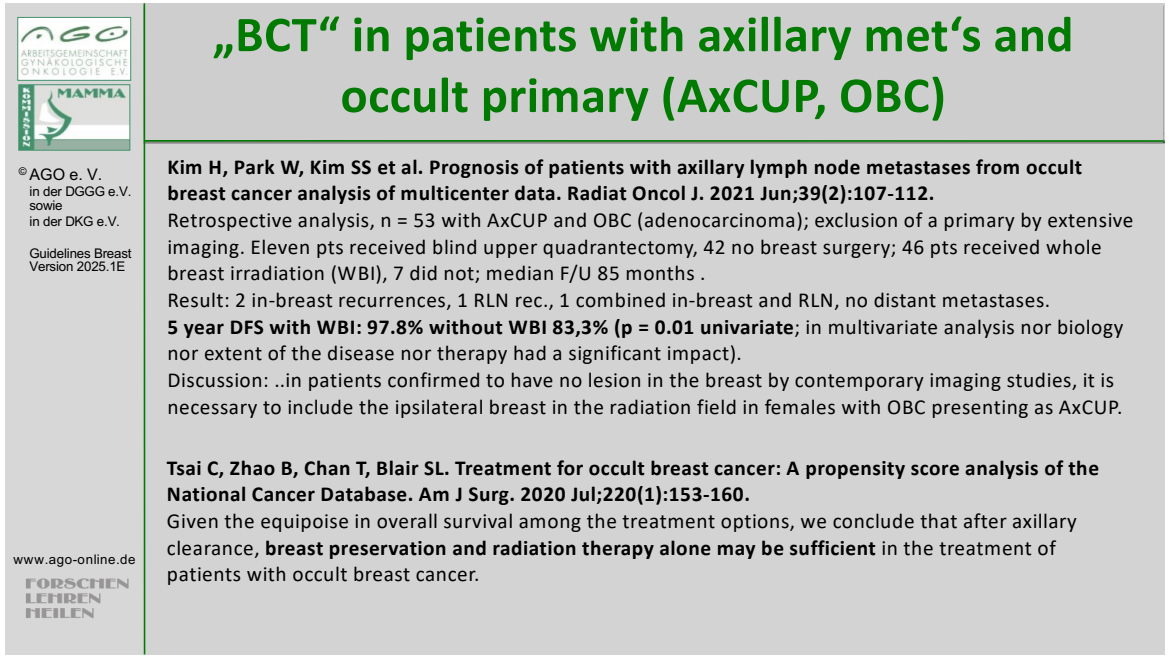
Statement: Breast irradiation if breast MRI is negative

1. Tsai C, Zhao B, Chan T, Blair SL. Treatment for occult breast cancer: A propensity score analysis of the National Cancer Database. Am J Surg. 2020 Jul;220(1):153-160.
2. Kim H, Park W, Kim SS et al. Prognosis of patients with axillary lymph node metastases from occult breast cancer: analysis of

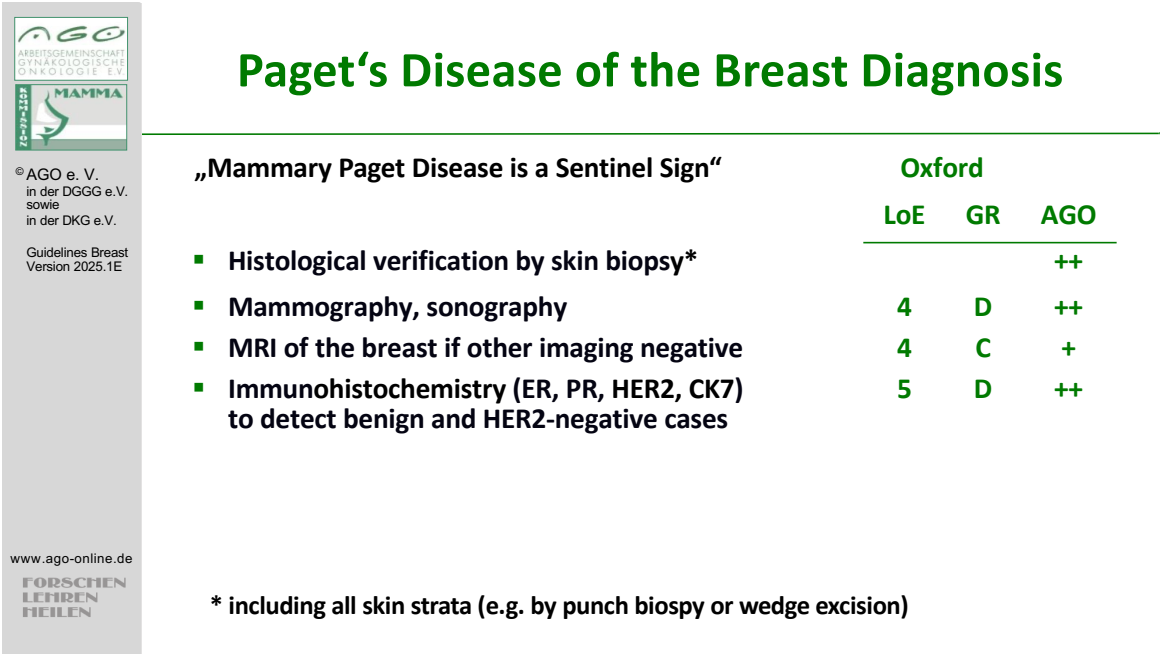
multicenter data. Radiat Oncol J. 2021 Jun;39(2):107-112.
3. Ofri A, Moore K. Occult breast cancer: Where are we at? Breast. 2020 Dec;54:211-215.
4. Hessler LK, Molitoris JK, Rosenblatt PY et al. Factors Influencing Management and Outcome in Patients with Occult Breast Cancer with Axillary Lymph Node Involvement: Analysis of the National Cancer Database. Surg Oncol 2017 Oct;24(10):2907-2914.
5. Barton, S. R., Smith, I. E., Kirby, et al. (2011). The role of ipsilateral breast radiotherapy in management of occult primary breast cancer presenting as axillary lymphadenopathy. European Journal of Cancer (Oxford, England : 1990), 47(14), 2099–2106. http://doi.org/10.1016/j.ejca.2011.05.010
6. Masinghe, S. P., Faluyi, O. O., Kerr, G. R., et al. (2011). Breast Radiotherapy for Occult Breast Cancer with Axillary Nodal Metastases - Does it Reduce the Local Recurrence Rate and Increase Overall Survival? Clinical Oncology (Royal College of Radiologists (Great Britain)), 23(2), 95–100.

<u>Statement: Systemic treatment according N+ tumor</u>

1. Pavlidis, N., Briasoulis, E., Hainsworth J. et al. (2003). Diagnostic and therapeutic management of cancer of an unknown primary. European Journal of Cancer (Oxford, England : 1990), 39(14), 1990–2005. http://doi.org/10.1016/S0959-8049(03)00547-1
2. Pentheroudakis, G., Lazaridis, G., & Pavlidis, N. (2010). Axillary nodal metastases from carcinoma of unknown primary (CUPAx): a systematic review of published evidence. Breast Cancer Research and Treatment, 119(1), 1–11. http://doi.org/10.1007/s10549-009-0554-3
3. Ofri A, Moore K. Occult breast cancer: Where are we at? Breast. 2020 Dec;54:211-215. doi: 10.1016/j.breast.2020.10.012. Epub 2020 Oct 27.



1. Kim H, Park W, Kim SS et al. Prognosis of patients with axillary lymph node metastases from occult breast cancer: analysis of multicenter data. Radiat Oncol J. 2021 Jun;39(2):107-112.
2. Tsai, C., Zhao, B., Chan, T. & Blair, S. L. Treatment for occult breast cancer: A propensity score analysis of the National Cancer Database. Am. J. Surg. 220, 153–160 (2020).



General recommendations / Guidelines:

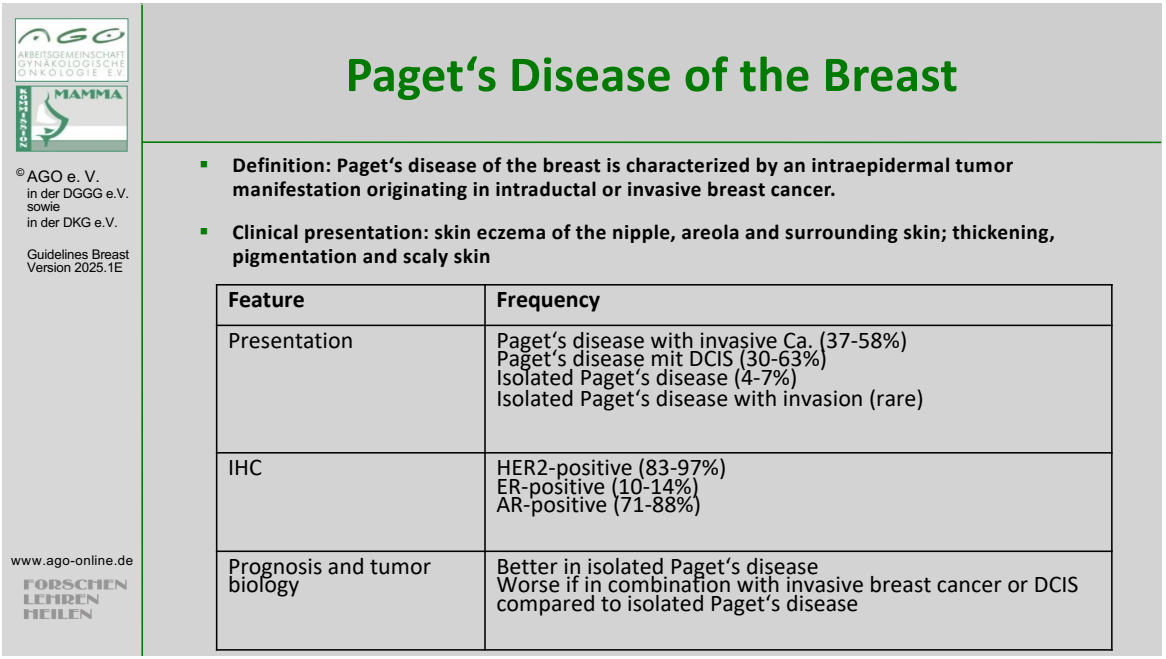
1. Mariano L, Nicosia L, Pupo D et al. A Pictorial Exploration of Mammary Paget Disease: Insights and Perspectives. Cancers (Basel). 2023 Nov 3;15(21):5276.
2. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (6.2024). Paget Disease (PAGET-1)

Imaging

1. Mariano L, Nicosia L, Pupo D et al. A Pictorial Exploration of Mammary Paget Disease: Insights and Perspectives. Cancers (Basel). 2023 Nov 3;15(21):5276.
2. 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
3. Capobianco, G., Spaliviero, B., Dessole, S., et al. (2006). Paget's disease of the nipple diagnosed by MRI. Archives of Gynecology and Obstetrics, 274(5), 316–318. http://doi.org/10.1007/s00404-006-0160-0
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
5. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (6.2024). Paget Disease (PAGET-1)

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
3. Sek, P., Zawrocki, A., Biernat, W., et al(2010). HER2 molecular subtype is a dominant subtype of mammary Paget's cells. An immunohistochemical study. Histopathology, 57(4), 564–571. http://doi.org/10.1111/j.1365-2559.2010.03665.x



Review

1. Streng A, Gutjahr E, Aulmann S, et al. Pathologie der Mamillenregion : I. Morbus Paget der Mamille, Varianten und Differenzialdiagnosen. *Der Pathologe*. 2020;29(4):14-399. doi:10.1007/s00292-020-00772-

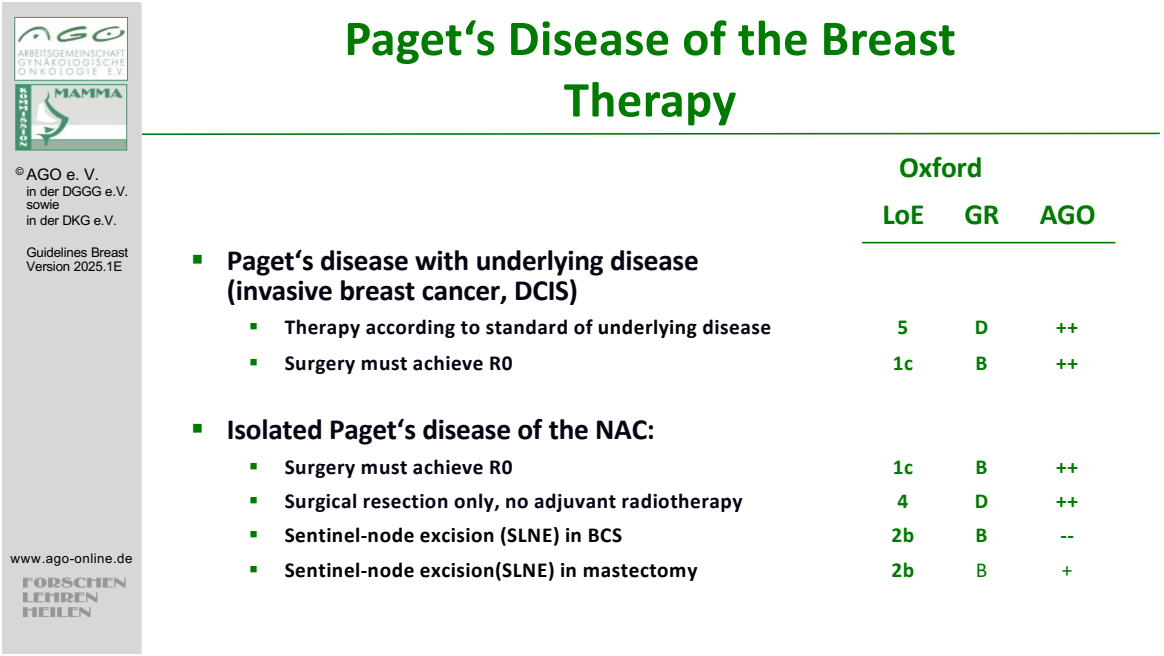
Clinical Presentation

1. 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
2. Onoe, S., Kinoshita, T., Tamura, N. et al. (2011). Feasibility of breast conserving surgery for Paget's disease. Breast (Edinburgh, Scotland), 20(6), 515–518. http://doi.org/10.1016/j.breast.2011.05.010
3. 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/1a0.1016/j.amjsurg.2009.07.044

Pathology and Immunohistochemistry

1. Lester, T., Wang, J., Bourne, P., et al. (2009). Different panels of markers should be used to predict mammary Paget's disease associated with in situ or invasive ductal carcinoma of the breast. Annals of Clinical and Laboratory Science, 39(1), 17–24.
2. Liegl, B., Horn, L.-C., & Moinfar, F. (2005). Androgen receptors are frequently expressed in mammary and extramammary Paget's

disease. Modern Pathology, 18(10), 1283–1288. http://doi.org/10.1038/modpathol.3800437
3. Sanders, M. A., Dominici, L., Denison, C., et al. (2013). Paget disease of the breast with invasion from nipple skin into the dermis: an unusual type of skin invasion not associated with an adverse outcome. Archives of Pathology & Laboratory Medicine, 137(1), 72–76. http://doi.org/10.5858/arpa.2011-0611-OA



Paget‘s Disease of the Breast
Therapy

	Oxford LoE	Oxford GR	Oxford AGO
Paget‘s disease with underlying disease (invasive breast cancer, DCIS)			
Therapy according to standard of underlying disease	5	D	++
Surgery must achieve R0	1c	B	++
Isolated Paget‘s disease of the NAC:			
Surgery must achieve R0	1c	B	++
Surgical resection only, no adjuvant radiotherapy	4	D	++
Sentinel-node excision (SLNE) in BCS	2b	B	--
Sentinel-node excision(SLNE) in mastectomy	2b	B	+

General recommendations / Guidelines:

1. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (6.2024). Paget Disease (PAGET-1)

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

1. Lin C-W, Chiang M-H, Tam K-W: Treatment of Mammary Paget Disease: A systematic review and meta-analysis of real-world data. Int J Surg 2022;107:106964.
2. Markarian S, Holmes DR: Mammary Paget's Disease: An Update. Cancers (Basel) 2022;14
3. 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.
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.2011.07.01

Treatment of isolated Pagets’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. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (6.2024). Paget Disease (PAGET-1)

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.
2. 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
3. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (6.2024). Paget Disease (PAGET-1)

Borderline and Malignant Phyllodes Tumor Diagnosis

	Oxford		
	LoE	GR	AGO
▪ **Mammography, sonography**	3	C	++
▪ **Diagnosis on core biopsy, grade determination on resection specimen**	3	C	++
▪ **Breast MRI**	3	C	+/-
▪ **Staging only malignant PT (CT thorax / abdomen, bone scan)**	5	D	++

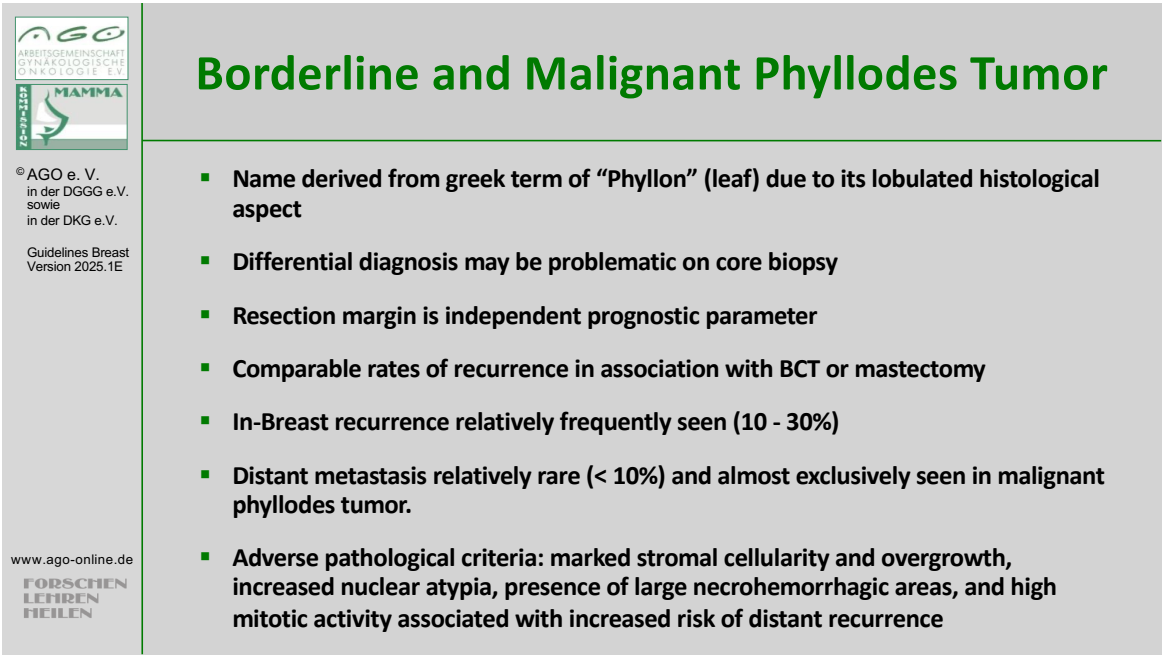
Guidelines:
1. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (6.2024). Phyllodes tumor (PHYLL-1)

Review
1. Ofri, A. et al. Diagnosis and management of phyllodes tumours for the surgeon: An algorithm. Surg. 20, e355–e365 (2022).

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

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. 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

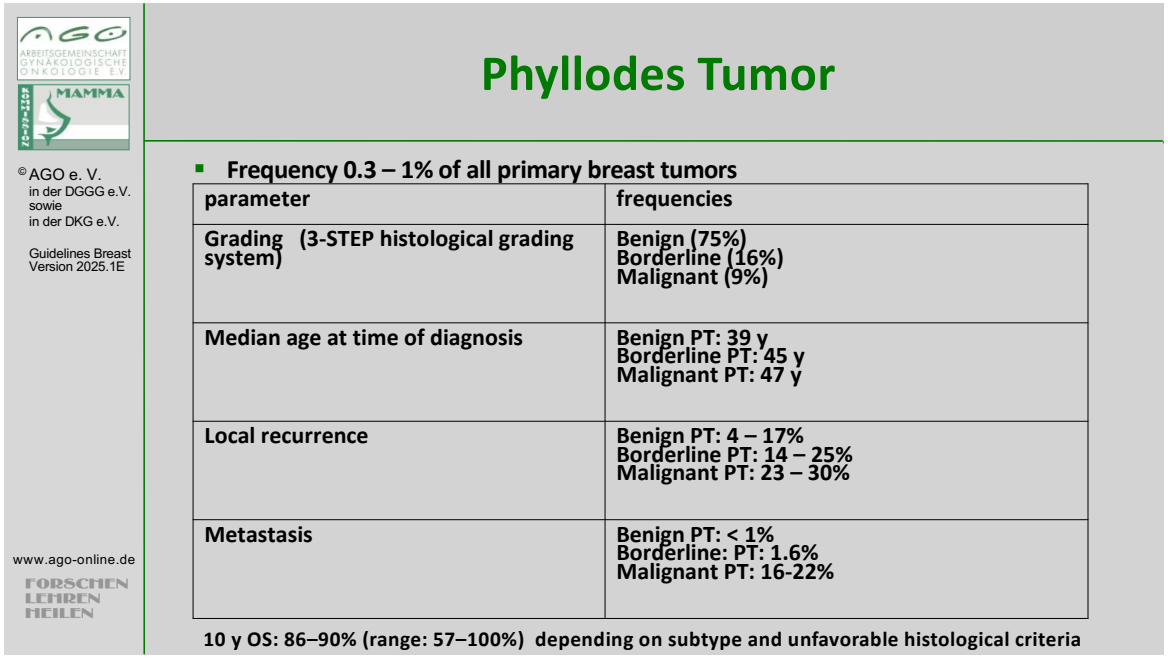


Review

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. 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
2. Chao X, Chen K, Zeng J, et al.: Adjuvant radiotherapy and chemotherapy for patients with breast phyllodes tumors: a systematic review and meta-analysis. BMC Cancer. 2019 Apr 23;19(1):372. doi: 10.1186/s12885-019-5585-5
3. Choi N, Kim K, Shin KH, et al.: The Characteristics of Local Recurrence After Breast-Conserving Surgery Alone for Malignant and Borderline Phyllodes Tumors of the Breast (KROG 16-08). Clin Breast Cancer. 2019 Oct;19(5):345-353.e2. doi: 10.1016/j.clbc.2019.04.003.
4. Lu Y, Chen Y, Zhu L, et al.: Local Recurrence of Benign, Borderline, and Malignant Phyllodes Tumors of the Breast: A Systematic Review and Meta-analysis. Ann Surg Oncol. 2019 May;26(5):1263-1275. doi: 10.1245/s10434-018-07134-5
5. Spanheimer PM, Murray MP, Zabor EC, et al.: Long-Term Outcomes After Surgical Treatment of Malignant/ Borderline Phyllodes Tumors of the Breast. Ann Surg Oncol (2019) 26:2136–2143 https://doi.org/10.1245/s10434-019-07210-4



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. 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
2. Chao X, Chen K, Zeng J, et al.: Adjuvant radiotherapy and chemotherapy for patients with breast phyllodes tumors: a systematic review and meta-analysis. BMC Cancer. 2019 Apr 23;19(1):372. doi: 10.1186/s12885-019-5585-5
3. Choi N, Kim K, Shin KH, et al.: The Characteristics of Local Recurrence After Breast-Conserving Surgery Alone for Malignant and Borderline Phyllodes Tumors of the Breast (KROG 16-08). Clin Breast Cancer. 2019 Oct;19(5):345-353.e2. doi: 10.1016/j.clbc.2019.04.003.
4. Lu Y, Chen Y, Zhu L, et al.: Local Recurrence of Benign, Borderline, and Malignant Phyllodes Tumors of the Breast: A Systematic Review and Meta-analysis. Ann Surg Oncol. 2019 May;26(5):1263-1275. doi: 10.1245/s10434-018-07134-5
5. Spanheimer PM, Murray MP, Zabor EC, et al.: Long-Term Outcomes After Surgical Treatment of Malignant/ Borderline Phyllodes Tumors of the Breast. Ann Surg Oncol (2019) 26:2136–2143 https://doi.org/10.1245/s10434-019-07210-4

Borderline and Malignant Phyllodes Tumor Surgery

	Oxford		
	LoE	GR	AGO
▪ **Fibroepithelial lesions with rapid growth or size > 3 cm should be excised (independently from the any CNB result)**	5	D	++
▪ **If the result of the CNB is unclear or suspicious for PT, excision with clear margins should be performed**	5	D	++
▪ **SLNE / Axillary dissection (if clinically unsuspicious)**	4	C	--
▪ **Treatment of local recurrence**			
▪ **R0 resection or simple mastectomy**	4	C	++

General recommendations / Guidelines:

1. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (6.2024). Phyllodes Tumor (Phyll-1)
2. Bogach J, Sriskandarajah A, Wright FC, et al.; Canadian Phyllodes Tumor Consensus Panel. Phyllodes Tumors of the Breast: Canadian National Consensus Document Using Modified Delphi Methodology. Ann Surg Oncol. 2023 Oct;30(11):6386-6397.
3. Louie AD, Rosenberger LH. Phyllodes Tumors of the Breast: Addressing the Gaps in Consensus Recommendations for Clinical Management. Ann Surg Oncol. 2023 Oct;30(11):6296-6298.
4. Goodwin B, Oyinlola AF, Palhang M et al.. Metastatic and Malignant Phyllodes Tumors of the Breast: An Update for Current Management. Am Surg. 2023 Aug 23:31348231198114.
5. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.
6. Sars C, Sackey H, Frisell J et al. Current clinical practice in the management of phyllodes tumors of the breast: an international cross-sectional study among surgeons and oncologists. Breast Cancer Res Treat. 2023 Jun;199(2):293-304.
7. Papas Y, Asmar AE, Ghandour F, Hajj I. Malignant phyllodes tumors of the breast: A comprehensive literature review. Breast J. 2020 Feb;26(2):240-244.
8. Lerwill, M. F., Lee, A. H. S. & Tan, P. H. Fibroepithelial tumours of the breast—a review. Virchows Arch. 480, 45–63 (2022).

Surgical margins: Observational study:

1. Ranjbar A, Zangouri V, Shokripour M. Margin status impact on recurrence of phyllodes tumors in high-risk groups: a retrospective observational study. BMC Cancer. 2024 Jan 9;24(1):48.

Surgical margins: Systematic review

1. Bogach J, Sriskandarajah A, Wright FC, et al. ; Canadian Phyllodes Tumor Consensus Panel. Phyllodes Tumors of the Breast: Canadian National Consensus Document Using Modified Delphi Methodology. Ann Surg Oncol. 2023 Oct;30(11):6386-6397.
2. Yu C-Y, Huang T-W, Tam K-W: Management of phyllodes tumor: A systematic review and meta-analysis of real-world evidence. Int J Surg 2022;107:106969.
3. Thind A, Patel B, Thind K, et al. Surgical margins for borderline and malignant phyllodes tumours. *Ann R Coll Surg Engl*. 2020;102(3):165-173. doi:10.1308/rcsann.2019.0140.
4. Lu Y, Chen Y, Zhu L, et al. Local Recurrence of Benign, Borderline, and Malignant Phyllodes Tumors of the Breast: A Systematic Review and Meta-analysis. *Ann Surg Oncol*. 2019;90:342–13. doi:10.1245/s10434-018-07134-5.
3. Rosenberger LH, Thomas SM, Nimbkar SN, et al.. Contemporary Multi-Institutional Cohort of 550 Cases of Phyllodes Tumors (2007-2017) Demonstrates a Need for More Individualized Margin Guidelines. J Clin Oncol. 21 Jan 20;39(3):178-189.

Operative management and prognosis of Phyllodes Tumors

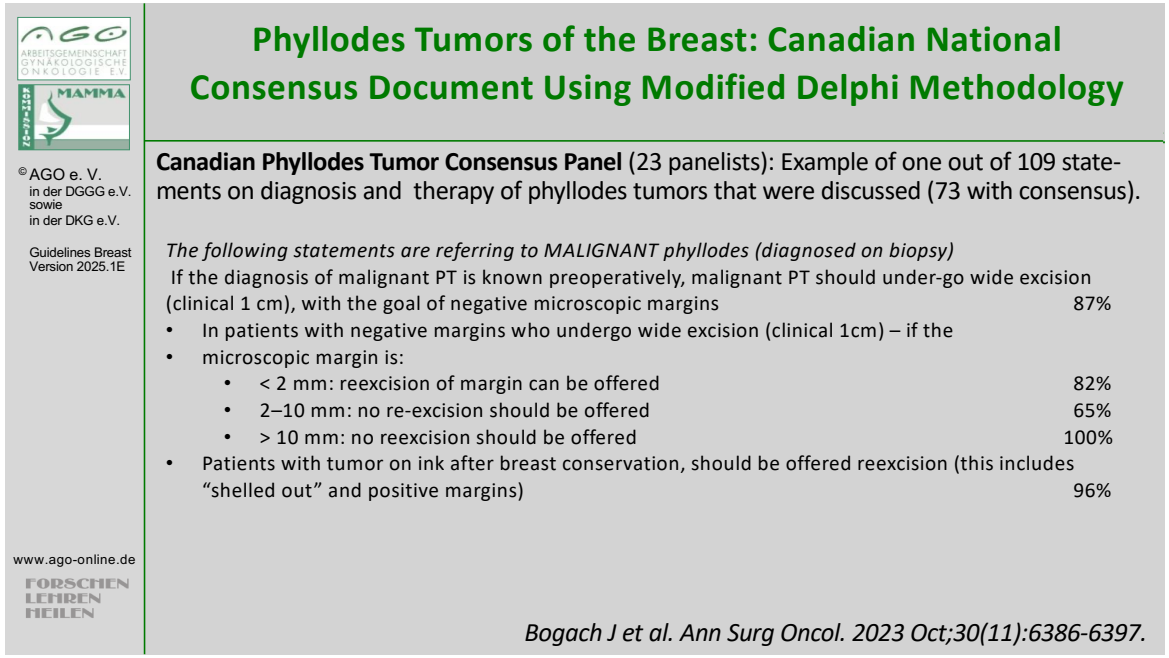
1. Bogach J, Sriskandarajah A, Wright FC, et al. ; Canadian Phyllodes Tumor Consensus Panel. Phyllodes Tumors of the Breast: Canadian National Consensus Document Using Modified Delphi Methodology. Ann Surg Oncol. 2023 Oct;30(11):6386-6397.
2. Macdonald, O. K., Lee, C. M., Tward, J. D., et al. (2006). 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
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
4. 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
5. Spanheimer PM, Murray MP, Zabor EC, et al.: Long-Term Outcomes After Surgical Treatment of Malignant/ Borderline Phyllodes Tumors of the Breast. Ann Surg Oncol (2019) 26:2136–2143 https://doi.org/10.1245/s10434-019-07210-4

Statement: SNE / Axillary dissection in cN0

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. 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



1. Bogach J, Sriskandarajah A, Wright FC, Look Hong N; Canadian Phyllodes Tumor Consensus Panel. Phyllodes Tumors of the Breast: Canadian National Consensus Document Using Modified Delphi Methodology. Ann Surg Oncol. 2023 Oct;30(11):6386-6397.

Borderline and Malignant Phyllodes Tumor
- Margins -

	Oxford LoE	Oxford GR	Oxford AGO
▪ **Intended lesion-free surgical margins are*** **- in borderline PT: ≥ 2 mm** **- in malignant PT: ≥ 10 mm**	**2b**	**B**	**++**
▪ **Intended pathologically lesion-free margins are*** **- in borderline PT: negative (no ink on ~~the~~ tumor)** **- in malignant PT: ≥ 2 mm**	**2b**	**B**	**++**
▪ **Re-resection recommended** **- in borderline PT: if margin* positive (ink on tumor)** **- in malignant PT: if margin < 2 mm**	**2b**	**B**	**++**

* Margins related to breast tissue only (but not to skin or to the thoracic wall)

General recommendations / Guidelines:

1. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (6.2024). Phyllodes Tumor (Phyll-1)
2. Bogach J, Sriskandarajah A, Wright FC, et al. Canadian Phyllodes Tumor Consensus Panel. Phyllodes Tumors of the Breast: Canadian National Consensus Document Using Modified Delphi Methodology. Ann Surg Oncol. 2023 Oct;30(11):6386-6397.
3. Louie AD, Rosenberger LH. Phyllodes Tumors of the Breast: Addressing the Gaps in Consensus Recommendations for Clinical Management. Ann Surg Oncol. 2023 Oct;30(11):6296-6298.
4. Goodwin B, Oyinlola AF, Palhang M et al.. Metastatic and Malignant Phyllodes Tumors of the Breast: An Update for Current Management. Am Surg. 2023 Aug 23:31348231198114.
5. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.
6. Sars C, Sackey H, Frisell J et al. Current clinical practice in the management of phyllodes tumors of the breast: an international cross-sectional study among surgeons and oncologists. Breast Cancer Res Treat. 2023 Jun;199(2):293-304.
7. Papas Y, Asmar AE, Ghandour F, Hajj I. Malignant phyllodes tumors of the breast: A comprehensive literature review. Breast J. 2020 Feb;26(2):240-244.
8. Lerwill, M. F., Lee, A. H. S. & Tan, P. H. Fibroepithelial tumours of the breast—a review. Virchows Arch. 480, 45–63 (2022).

Surgical margins: Observational study:

1. Ranjbar A, Zangouri V, Shokripour M. Margin status impact on recurrence of phyllodes tumors in high-risk groups: a retrospective observational study. BMC Cancer. 2024 Jan 9;24(1):48.

Surgical margins: Systematic review

1. Yu C-Y, Huang T-W, Tam K-W: Management of phyllodes tumor: A systematic review and meta-analysis of real-world evidence. Int J Surg 2022;107:106969.
2. Thind A, Patel B, Thind K, et al. Surgical margins for borderline and malignant phyllodes tumours. *Ann R Coll Surg Engl*. 2020;102(3):165-173. doi:10.1308/rcsann.2019.0140.
3. Lu Y, Chen Y, Zhu L, et al. Local Recurrence of Benign, Borderline, and Malignant Phyllodes Tumors of the Breast: A Systematic Review and Meta-analysis. *Ann Surg Oncol*. 2019;90:342–13. doi:10.1245/s10434-018-07134-5.
3. Rosenberger LH, Thomas SM, Nimbkar SN, et al.. Contemporary Multi-Institutional Cohort of 550 Cases of Phyllodes Tumors (2007-2017) Demonstrates a Need for More Individualized Margin Guidelines. J Clin Oncol. 21 Jan 20;39(3):178-189.

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. 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
3. 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
4. Spanheimer PM, Murray MP, Zabor EC, et al.: Long-Term Outcomes After Surgical Treatment of Malignant/ Borderline Phyllodes Tumors of the Breast. Ann Surg Oncol (2019) 26:2136–2143 https://doi.org/10.1245/s10434-019-07210-4

Statement: SNE / Axillary dissection in cN0

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. 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

Borderline and Malignant Phyllodes Tumor
- Adjuvant Radiotherapy -

Adjuvant radiotherapy of the breast and the thoracic wall is aimed at local control.

	Oxford LoE	Oxford GR	Oxford AGO
▪ **BCS, R0-resection** - Borderline PT: no - Malignant PT: yes (independently from the size of the lesion)	2b	B	+
▪ **Mastectomy, R0-resection** - Borderline PT: no - Malignant PT: < 5 cm: no - Malignant PT: ≥ 5 cm: with aggressive pathology or growth	2b	B	+
▪ **Mastectomy, R1-resection** - Borderline PT: no - Maligner PT: ja (independently from the size of the lesion)	2b	B	+

General recommendations / Guidelines:

1. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (6.2024). Phyllodes Tumor (Phyll-1)
2. Bogach J, Sriskandarajah A, Wright FC, et al.; Canadian Phyllodes Tumor Consensus Panel. Phyllodes Tumors of the Breast: Canadian National Consensus Document Using Modified Delphi Methodology. Ann Surg Oncol. 2023 Oct;30(11):6386-6397.
3. Louie AD, Rosenberger LH. Phyllodes Tumors of the Breast: Addressing the Gaps in Consensus Recommendations for Clinical Management. Ann Surg Oncol. 2023 Oct;30(11):6296-6298.
4. Goodwin B, Oyinlola AF, Palhang M et al.. Metastatic and Malignant Phyllodes Tumors of the Breast: An Update for Current Management. Am Surg. 2023 Aug 23:31348231198114.
5. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.
6. Sars C, Sackey H, Frisell J et al. Current clinical practice in the management of phyllodes tumors of the breast: an international cross-sectional study among surgeons and oncologists. Breast Cancer Res Treat. 2023 Jun;199(2):293-304.
7. Papas Y, Asmar AE, Ghandour F, Hajj I. Malignant phyllodes tumors of the breast: A comprehensive literature review. Breast J. 2020 Feb;26(2):240-244.
8. Chen, C., Huang, X., Xu, Y. & Sun, Q. Rethinking on the management strategy of malignant phyllodes tumor of the breast: An analysis based on the SEER database. Medicine 102, e33326 (2023).

Surgical margins: Systematic review

1. Yu C-Y, Huang T-W, Tam K-W: Management of phyllodes tumor: A systematic review and meta-analysis of real-world evidence. Int J Surg 2022;107:106969.
2. Thind A, Patel B, Thind K, et al. Surgical margins for borderline and malignant phyllodes tumours. *Ann R Coll Surg Engl*. 2020;102(3):165-173. doi:10.1308/rcsann.2019.0140.
3. Lu Y, Chen Y, Zhu L, et al. Local Recurrence of Benign, Borderline, and Malignant Phyllodes Tumors of the Breast: A Systematic Review and Meta-analysis. *Ann Surg Oncol*. 2019;90:342–13. doi:10.1245/s10434-018-07134-5.
3. Rosenberger LH, Thomas SM, Nimbkar SN, et al.. Contemporary Multi-Institutional Cohort of 550 Cases of Phyllodes Tumors (2007-2017) Demonstrates a Need for More Individualized Margin Guidelines. J Clin Oncol. 21 Jan 20;39(3):178-189.

Operative management and prognosis of Phyllodes Tumors

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2. 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
3. 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
4. Spanheimer PM, Murray MP, Zabor EC, et al.: Long-Term Outcomes After Surgical Treatment of Malignant/ Borderline Phyllodes Tumors of the Breast. Ann Surg Oncol (2019) 26:2136–2143 https://doi.org/10.1245/s10434-019-07210-4

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2. 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

Borderline and Malignant Phyllodes Tumor
Systemic Adjuvant Therapy

Guidelines Breast
Version 2025.1E

	Oxford		
	LoE	GR	AGO
Systemic adjuvant therapy (chemo, endocrine)			
Adjuvant endocrine therapy (irrespect. of ER/PR)	4	C	-
Adjuvant chemotherapy	4	C	-
Primary systemic therapy, if complete resection (R0) presumably cannot be achieved (Adriamycin/Ifosfamid)	4	C	+
Adjuvant Treatment of local recurrence			
Radiotherapy, chemotherapy after R1 resection	4	C	+/-
Distant metastasis (very rare)			
Multidisciplinary case discussion („Sarcoma board“)	5	D	++
Treatment like soft tissue sarcomas	4	C	++
Surgical resection of metastatic lesions	4	C	+

General recommendations / Guidelines:

1. Breast Cancer. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). (6.2024). Phyllodes Tumor (Phyll-1)
2. Bogach J, Sriskandarajah A, Wright Fcet al.; Canadian Phyllodes Tumor Consensus Panel. Phyllodes Tumors of the Breast: Canadian National Consensus Document Using Modified Delphi Methodology. Ann Surg Oncol. 2023 Oct;30(11):6386-6397.
3. Louie AD, Rosenberger LH. Phyllodes Tumors of the Breast: Addressing the Gaps in Consensus Recommendations for Clinical Management. Ann Surg Oncol. 2023 Oct;30(11):6296-6298.
4. Goodwin B, Oyinlola AF, Palhang M et al.. Metastatic and Malignant Phyllodes Tumors of the Breast: An Update for Current Management. Am Surg. 2023 Aug 23:31348231198114.
5. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.
6. Sars C, Sackey H, Frisell J et al. Current clinical practice in the management of phyllodes tumors of the breast: an international cross-sectional study among surgeons and oncologists. Breast Cancer Res Treat. 2023 Jun;199(2):293-304.
7. Papas Y, Asmar AE, Ghandour F, Hajj I. Malignant phyllodes tumors of the breast: A comprehensive literature review. Breast J. 2020 Feb;26(2):240-244.
8. Chen, C., Huang, X., Xu, Y. & Sun, Q. Rethinking on the management strategy of malignant phyllodes tumor of the breast: An analysis based on the SEER database. Medicine 102, e33326 (2023).

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. 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
4. Chao X, Chen K, Zeng J, et al. Adjuvant radiotherapy and chemotherapy for patients with breast phyllodes tumors: a systematic review and meta-analysis. BMC Cancer. 2019;19(1):372. Published 2019 Apr 23. doi:10.1186/s12885-019-5585-5
5. Sars C, Sackey H, Frisell J et al. Current clinical practice in the management of phyllodes tumors of the breast: an international cross-sectional study among surgeons and oncologists. Breast Cancer Res Treat. 2023 Jun;199(2):293-304. doi: 10.1007/s10549-023-06896-1. Epub 2023 Mar 6. PMID: 36879102; PMCID: PMC9988205.
6. Gutnik L, Ren Y, Thomas SM et al. Malignant phyllodes tumor and primary breast sarcoma; distinct rare tumors of the breast. J Surg Oncol. 2022 May;125(6):947-957. doi: 10.1002/jso.26820. Epub 2022 Feb 18. PMID: 35179788; PMCID: PMC8995353.

Statement: Adjuvant radiotherapy

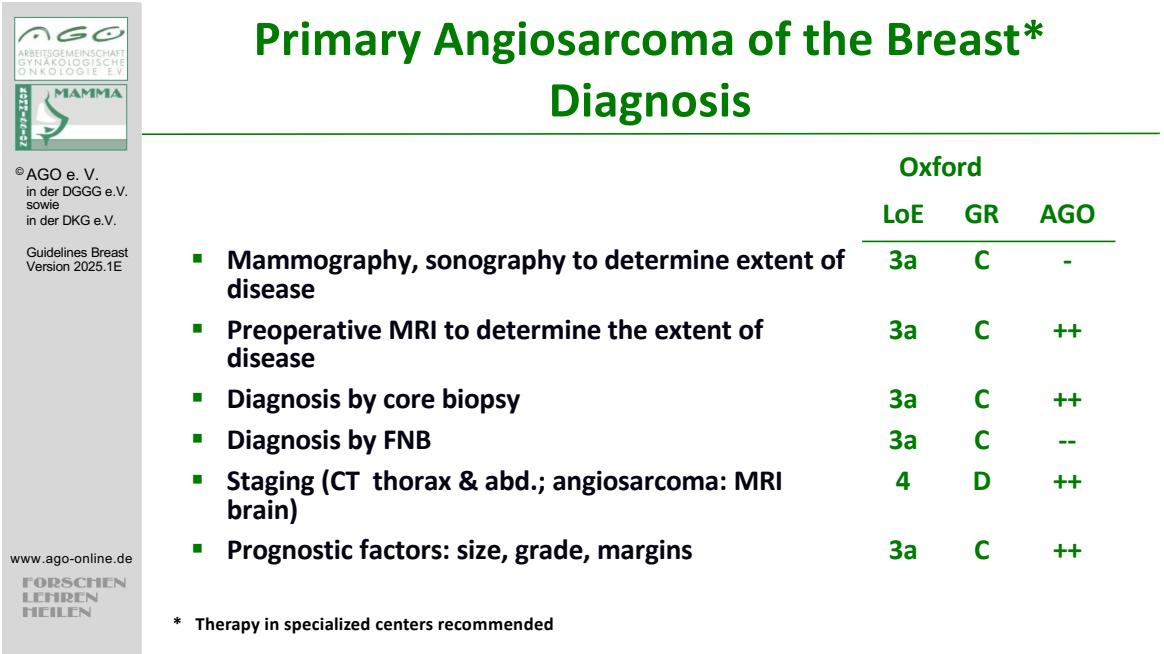
1. Kim, Y.-J., & Kim, K. (2017). Radiation therapy for malignant phyllodes tumor of the breast: An analysis of SEER data. Breast (Edinburgh, Scotland), 32, 26–32. http://doi.org/10.1016/j.breast.2016.12.006
2. Choi, N., Kim, K., Shin, K.H., et al. (2018). Malignant and borderline phyllodes tumors of 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.
3. Chao X, Chen K, Zeng J, et al.: Adjuvant radiotherapy and chemotherapy for patients with breast phyllodes tumors: a systematic review and meta-analysis. BMC Cancer. 2019 Apr 23;19(1):372. doi: 10.1186/s12885-019-5585-5.
4. Choi N, Kim K, Shin KH, et al.: The Characteristics of Local Recurrence After Breast-Conserving Surgery Alone for Malignant and Borderline Phyllodes Tumors of the Breast (KROG 16-08). Clin Breast Cancer. 2019 Oct;19(5):345-353.e2. doi: 10.1016/j.clbc.2019.04.003.
5. Lu Y, Chen Y, Zhu L, et al.: Local Recurrence of Benign, Borderline, and Malignant Phyllodes Tumors of the Breast: A Systematic Review and Meta-analysis. Ann Surg Oncol. 2019 May;26(5):1263-1275. doi: 10.1245/s10434-018-07134-5.

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: 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
3. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf Version 5.2023
4. Samii E, Hurni Y, Huber D. Management and Outcomes of Metastatic and Recurrent Malignant Phyllodes Tumors of the Breast: A Systematic Literature Review. Eur J Breast Health. 2023 Jul 3;19(3):191-200.



Primary Angiosarcoma of the Breast*
Diagnosis

	Oxford		
	LoE	GR	AGO
▪ Mammography, sonography to determine extent of disease	3a	C	-
▪ Preoperative MRI to determine the extent of disease	3a	C	++
▪ Diagnosis by core biopsy	3a	C	++
▪ Diagnosis by FNB	3a	C	--
▪ Staging (CT thorax & abd.; angiosarcoma: MRI brain)	4	D	++
▪ Prognostic factors: size, grade, margins	3a	C	++

* Therapy in specialized centers recommended

Review

1. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.

Imaging

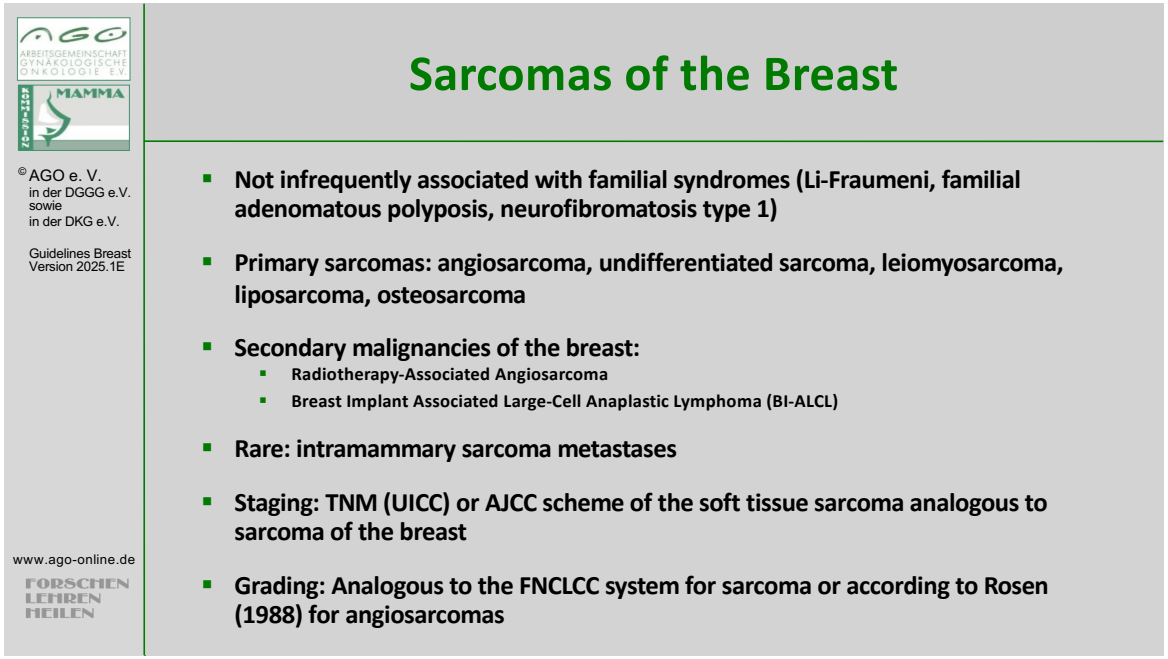
1. Glazebrook, K. N., Magut, M. J., & Reynolds, C. (2008). Angiosarcoma of the breast. American Journal of Roentgenology, 190(2), 533–538. http://doi.org/10.2214/AJR.07.2909
2. O'Neill, A. C., D'Arcy, C., McDermott, E., et al. (2014). Magnetic resonance imaging appearances in primary and secondary angiosarcoma of the breast. Journal of Medical Imaging and Radiation Oncology, 58(2), 208–212. http://doi.org/10.1111/1754-9485.12100
3. Chikarmane, S. A., Gombos, E. C., Jagadeesan, J., et al. (2015). MRI findings of radiation-associated angiosarcoma of the breast (RAS). J Magn Reson Imaging, 42(3), 763–770. http://doi.org/10.1002/jmri.24822
4. Yang, W. T., Hennessy, B. T. J., Dryden, M. J., et al. (2007). Mammary angiosarcomas: imaging findings in 24 patients. Radiology, 242(3), 725–734. http://doi.org/10.1148/radiol.2423060163

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. http://doi.org/10.1097/PAS.0b013e318176dbc7
2. Adem, C., Reynolds, C., Ingle, J. N., et al. (2004). Primary breast sarcoma: clinicopathologic series from the Mayo Clinic and review of the literature. British Journal of Cancer, 91(2), 237–241. http://doi.org/10.1038/sj.bjc.6601920
3. Udager, A. M., Ishikawa, M. K., Lucas, D. R., et al. (2016). MYC immunohistochemistry in angiosarcoma and atypical vascular lesions: practical considerations based on a single institutional experience. Pathology, 48(7), 697–704. http://doi.org/10.1016/j.pathol.2016.08.007

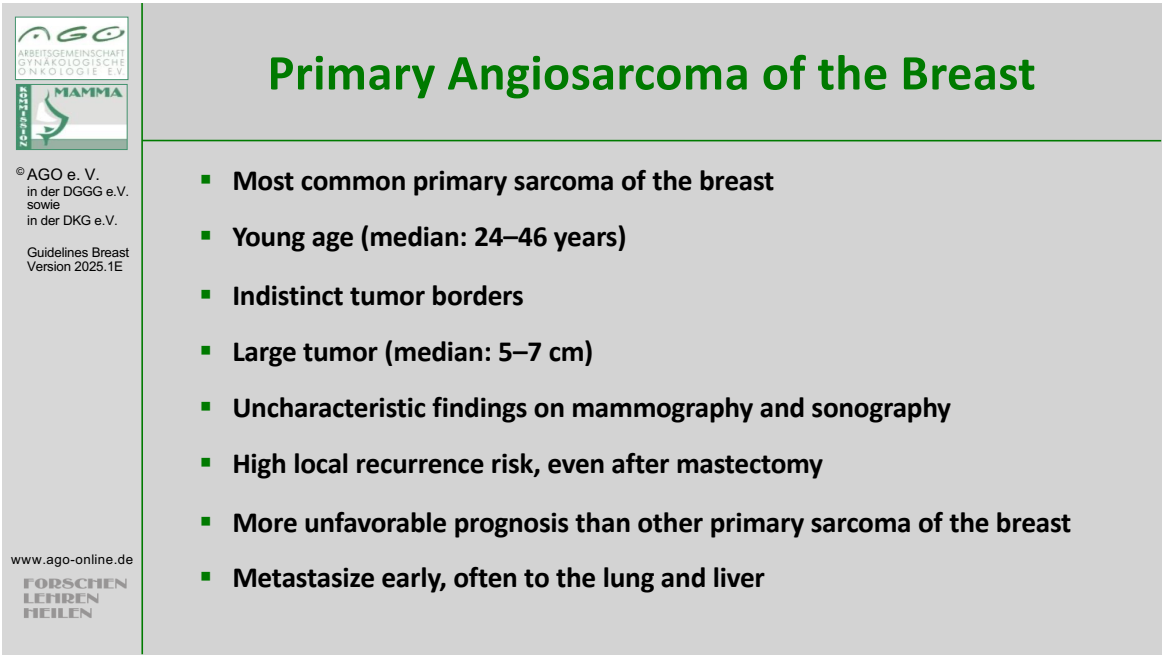
Prognostic Factors

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
2. Wang, X. Y., Jakowski, J., Tawfik, O. W., et al. (2009). Angiosarcoma of the breast: a clinicopathologic analysis of cases from the last 10 years. Annals of Diagnostic Pathology, 13(3), 147–150. http://doi.org/10.1016/j.anndiagpath.2009.02.001
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.



1. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.
2. Li W, Zhang S, Fan W, et al.: Sonographic imaging features of alveolar soft part sarcoma: Case series and literature review. Medicine (Baltimore) 2022;101:e31905.
3. 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
4. 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
5. 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
6. Penel, N., Marréaud, S., Robin, Y.-M. et al. (2011). Angiosarcoma: state of the art and perspectives. Critical Reviews in Oncology/Hematology, 80(2), 257–263. http://doi.org/10.1016/j.critrevonc.2010.10.007
7. 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
8. Young, R. J., Brown, N. J., Reed, M. W., et al. (2010). Angiosarcoma. The Lancet Oncology, 11(10), 983–991. http://doi.org/10.1016/S1470-2045(10)70023-1

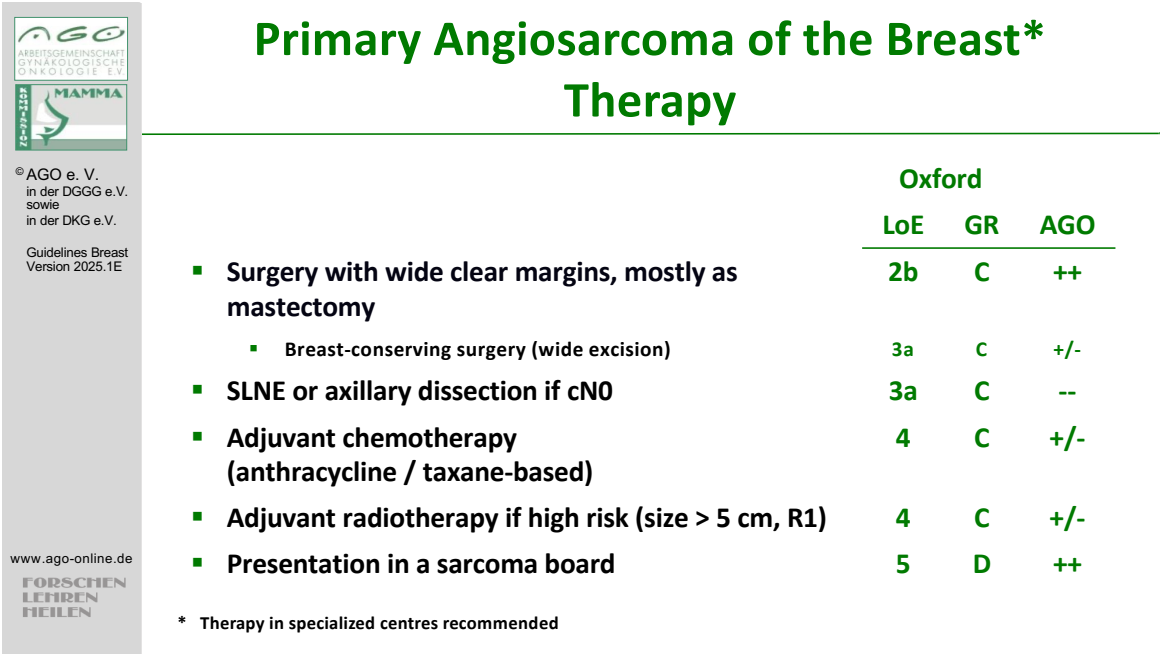
9. Hodgson, N. C., Bowen-Wells, C., Moffat, F. et al. (2007). Angiosarcomas of the breast: a review of 70 cases. American Journal of Clinical Oncology, 30(6), 570–573. http://doi.org/10.1097/COC.0b013e3181131d62



Reviews

1. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.
2. Sato, F. & Yamamoto, T. Breast angiosarcoma after primary breast cancer surgery: A systematic review. J Plastic Reconstr Aesthetic Surg 75, 2882–2889(2022).
3. 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.
4. 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.
5. Penel, N., Marréaud, S., Robin, Y.-M. et al. (2011). Angiosarcoma: state of the art and perspectives. Critical Reviews in Oncology/Hematology, 80(2), 257–263. http://doi.org/10.1016/j.critrevonc.2010.10.007
6. 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
7. Kunkiel, M., Maczkiewicz, M., Jagiello-Gruszfeld, 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.
8. Friedrich AU, Reisenbichler ES, Heller DR, et al. Characteristics and Long-Term Risk of Breast Angiosarcoma. Ann Surg Oncol. 2021

Sep;28(9):5112-5118.
9. Zhu Y, Nakamoto S, Tsukioki T, et al. Primary angiosarcoma of the breast: a literature review. Chin Clin Oncol. 2024 Oct;13(5):68. doi: 10.21037/cco-24-16. Epub 2024 Sep 5. PMID: 39260429.



Primary Angiosarcoma of the Breast* Therapy

	Oxford LoE	Oxford GR	Oxford AGO
▪ **Surgery with wide clear margins, mostly as mastectomy**	**2b**	**C**	**++**
▪ Breast-conserving surgery (wide excision)	3a	C	+/-
▪ **SLNE or axillary dissection if cN0**	**3a**	**C**	**--**
▪ **Adjuvant chemotherapy (anthracycline / taxane-based)**	**4**	**C**	**+/-**
▪ **Adjuvant radiotherapy if high risk (size > 5 cm, R1)**	**4**	**C**	**+/-**
▪ **Presentation in a sarcoma board**	**5**	**D**	**++**

* **Therapy in specialized centres recommended**

Reviews / Guidelines

1. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.
2. Zhu Y, Nakamoto S, Tsukioki T, et al. Primary angiosarcoma of the breast: a literature review. Chin Clin Oncol. 2024 Oct;13(5):68. doi: 10.21037/cco-24-16. Epub 2024 Sep 5. PMID: 39260429.
3. Palassini E, Baldi GG, Sulfaro S, et al. Clinical recommendations for treatment of localized angiosarcoma: A consensus paper by the Italian Sarcoma Group. Cancer Treat Rev. 2024 May;126:102722. doi: 10.1016/j.ctrv.2024.102722. Epub 2024 Mar 30. PMID: 38604052.

Surgery

1. Sato F, Yamamoto T: Breast angiosarcoma after primary breast cancer surgery: A systematic review. J Plast Reconstr Aesthet Surg 2022;75:2882–2889.
2. 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
3. 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

4. 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
5. Mitin T, McClelland S, Hatfield J, et al.: Impact of the extent of resection on primary breast angiosarcoma survival. ASCO 2019, abstr. 521

Adjuvant Treatment (Chemotherapy, 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. Sher, T., Hennessy, B. T., Valero, V., et al. (2007). Primary angiosarcomas of the breast. Cancer, 110(1), 173–178. http://doi.org/10.1002/cncr.22784
3. Schlemmer, M., Reichardt, P., Verweij, J., et al. (2008). Paclitaxel in patients with advanced angiosarcomas of soft tissue: a retrospective study of the EORTC soft tissue and bone sarcoma group. European Journal of Cancer (Oxford, England : 1990), 44(16), 2433–2436. http://doi.org/10.1016/j.ejca.2008.07.037
4. Teng L, Yan S, Du J, et al.. Clinicopathological analysis and prognostic treatment study of angiosarcoma of the breast: a SEER population-based analysis. World J Surg Oncol. 2023 May 9;21(1):144. doi: 10.1186/s12957-023-03030-9. PMID: 37158932; PMCID: PMC10169469

Secondary Angiosarcoma of the Breast Therapy

	Oxford		
	LoE	GR	AGO
▪ **Tumor resection (BCT / mastectomy)**	3a	C	+
Radical surgery ist not associated with better outcome			
▪ **(Neo-)adjuvant chemotherapy**	3a	C	+/-
▪ **Consider „trimodality treatment“ in case of locally advanced angiosarcoma (neoadjuvant taxanes => neoadjuvant radiochemotherapy => surgical resektion)**	3a	C	+
▪ **Adjuvant radiotherapy if high risk (size > 5 cm, R1)**	2b	B	+/-
▪ **Regional hyperthermia (to improve local control) plus chemotherapy and / or radiotherapy**	2b	B	+/-

Review / Guidelines

1. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.
2. Palassini E, Baldi GG, Sulfaro S, et al. Clinical recommendations for treatment of localized angiosarcoma: A consensus paper by the Italian Sarcoma Group. Cancer Treat Rev. 2024 May;126:102722. doi: 10.1016/j.ctrv.2024.102722. Epub 2024 Mar 30. PMID: 38604052

Surgery (BEO/mastectomy)

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
3. https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Adulte_Weichgewebesarkome/LL_Weichgewebesarkome_Langversion_1.0.pdf
4. Cohen-Hallaleh RB, Smith HG, Smith RC, et al. Radiation induced angiosarcoma of the breast: outcomes from a retrospective case

series. Clin Sarcoma Res. 2017 Aug 7;7:15. doi: 10.1186/s13569-017-0081-7.

(Neo-)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
2. 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
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
4. Perez-Ruiz, E., Ribelles, N., Sanchez-Muñoz, A., et al. (2009). Response to paclitaxel in a radiotherapy-induced breast angiosarcoma. Acta Oncologica, 48(7), 1078–1079. http://doi.org/10.1080/02841860902777115
5. 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
6. Schlemmer, M., Reichardt, P., Verweij, Jet al. (2008). Paclitaxel in patients with advanced angiosarcomas of soft tissue: a retrospective study of the EORTC soft tissue and bone sarcoma group. European Journal of Cancer (Oxford, England : 1990), 44(16), 2433–2436. http://doi.org/10.1016/j.ejca.2008.07.037
7. Cohen-Hallaleh RB, Smith HG, Smith RC, et al. Radiation induced angiosarcoma of the breast: outcomes from a retrospective case series. Clin Sarcoma Res. 2017 Aug 7;7:15. doi: 10.1186/s13569-017-0081-7.

Trimodale Therapie (Mayo)

1. Degnim AC, Siontis BL, Ahmed SK et al.. Trimodality Therapy Improves Disease Control in Radiation-Associated Angiosarcoma of the Breast. Clin Cancer Res. 2023 Aug 1;29(15):2885-2893.

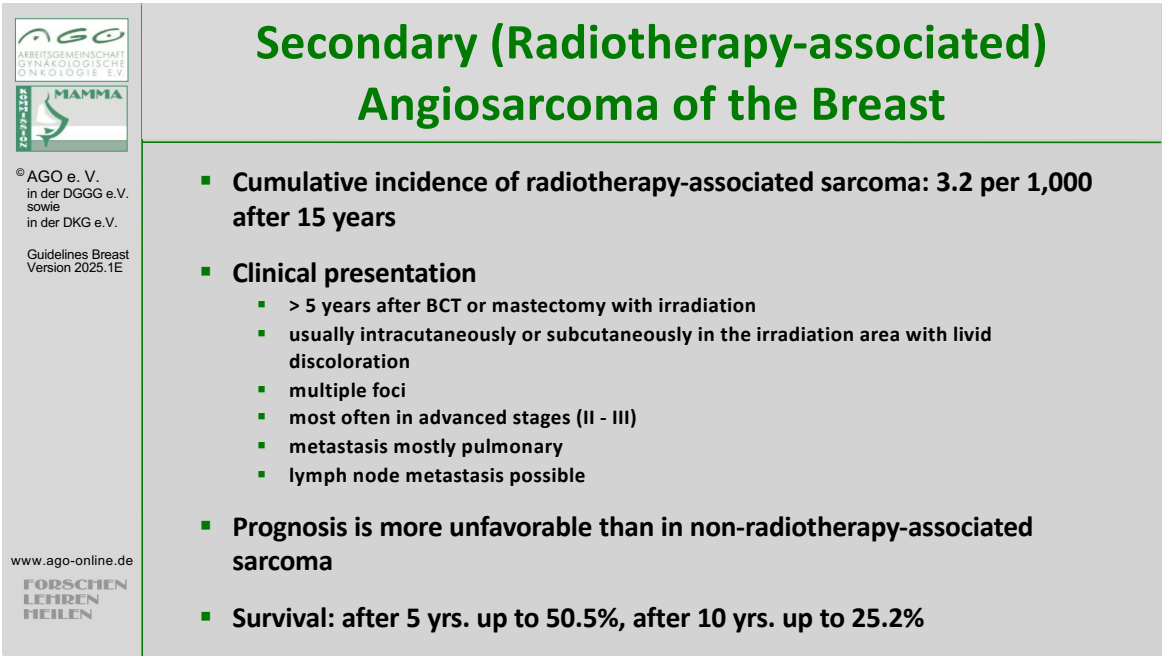
Adjuvant Radiotherapy

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
2. 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
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
4. Mathis, S. (2010). Hyperthermie. Systematischer Review. Ludwig Boltzmann Institut (pp. 1–59). http://eprints.hta.lbg.ac.at/883/1/DSD_36.pdf
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



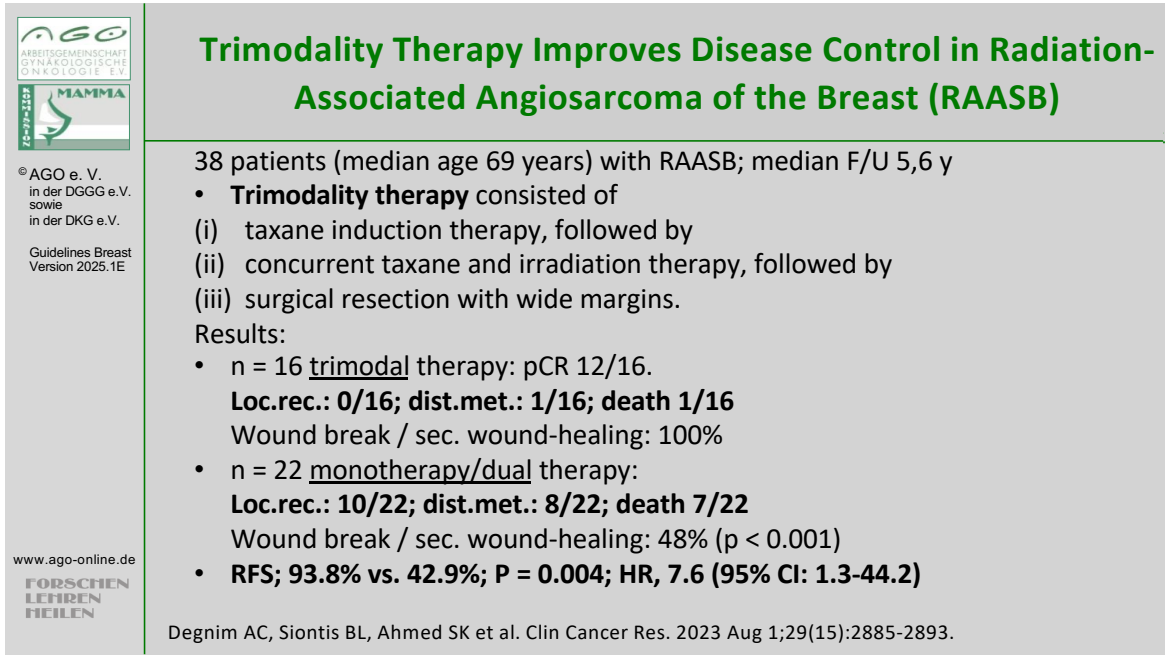
Review / Guidelines

1. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.
2. Palassini E, Baldi GG, Sulfaro S, et al. Clinical recommendations for treatment of localized angiosarcoma: A consensus paper by the Italian Sarcoma Group. Cancer Treat Rev. 2024 May;126:102722. doi: 10.1016/j.ctrv.2024.102722. Epub 2024 Mar 30. PMID: 38604052

Radiotherapy

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
3. D'Angelo, S. P., Antonescu, C. R., Kuk, D., et al. (2013). High-risk features in radiation-associated breast angiosarcomas. British Journal of Cancer, 109(9), 2340–2346. http://doi.org/10.1038/bjc.2013.590
4. 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
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
6. Scow, J. S., Reynolds, C. A., Degnim, A. C., et al. (2010). Primary and secondary angiosarcoma of the breast: the Mayo Clinic experience. Journal of Surgical Oncology, 101(5), 401–407. http://doi.org/10.1002/jso.21497
7. 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
8. 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.
9. Friedrich AU, Reisenbichler ES, Heller DR et al. Characteristics and Long-Term Risk of Breast Angiosarcoma. Ann Surg Oncol. 2021 Sep;28(9):5112-5118. doi: 10.1245/s10434-021-09689-2. Epub 2021 Feb 18.



Trimodality Therapy (Mayo)

1. Degnim AC, Siontis BL, Ahmed SK et al.. Trimodality Therapy Improves Disease Control in Radiation-Associated Angiosarcoma of the Breast. Clin Cancer Res. 2023 Aug 1;29(15):2885-2893.

Angiosarcoma of the Breast
Treatment of Local Recurrence and Metastases

	Oxford		
	LoE	GR	AGO
Treatment of Local Recurrence:			
▪ R0 resection	4	C	++
▪ Adjuvant radiotherapy for high-risk patients (tumor size > 5 cm, R1)	4	C	+/-
Distant Metastases / Unresectable Tumors:			
▪ Treatment like as for soft tissue sarcomas (according to S3 guideline)	4	C	++
▪ Paclitaxel weekly / liposomal doxorubicin (as in angiosarcoma)	2b	B	+
▪ Antiangiogenic treatment (e.g. in angiosarcoma)	4	C	+/-
If clinically resistant to therapy			
▪ Molecular diagnostics (Multidisciplinary molecular board)	5	D	+

Review

1. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.

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
3. https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Adulte_Weichgewebesarkome/LL_Weichgewebesarkome_Langversion_1.0.pdf

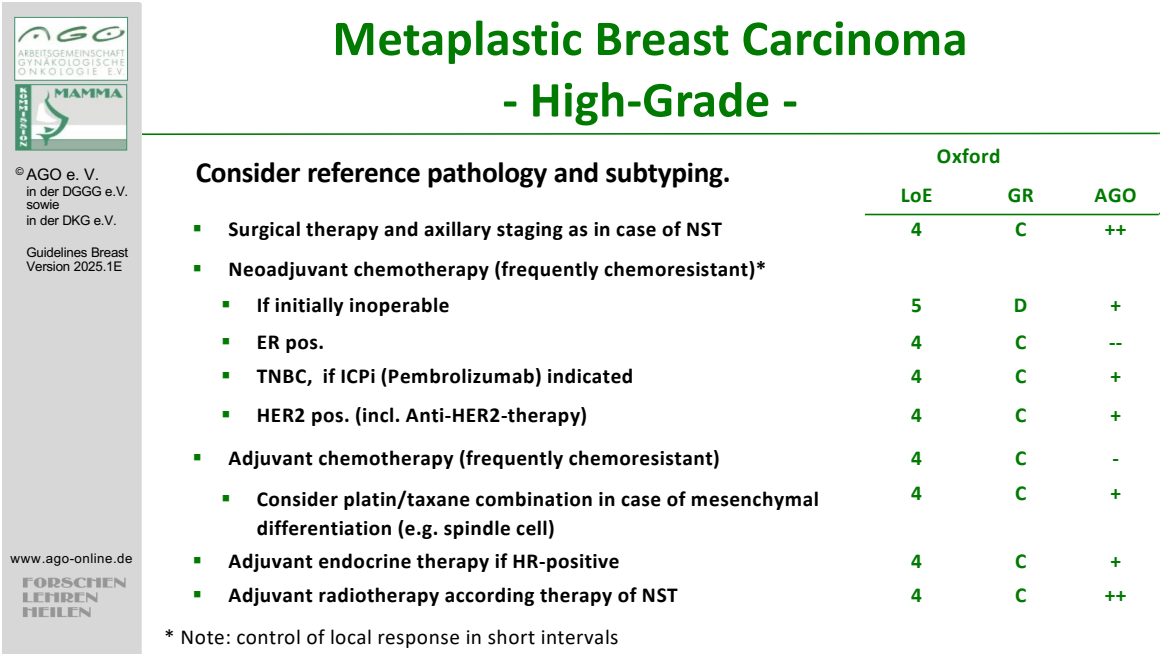
Treatment of metastatic and non-resectable tumors

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
2. Gatcombe, H. G., Olson, T. A., & Esiashvili, N. (2010). Metastatic primary angiosarcoma of the breast in a pediatric patient with a complete response to systemic chemotherapy and definitive radiation therapy: case report and review of the literature. Journal of Pediatric Hematology/Oncology, 32(3), 192–194. http://doi.org/10.1097/MPH.0b013e3181ca9ed7
3. Gambini, D., Visintin, R., Locatelli, E., et al. (2009). Paclitaxel-dependent prolonged and persistent complete remission four years from first recurrence of secondary breast angiosarcoma. Tumori, 95(6), 828–831.
4. Ray-Coquard IL, Domont J, Tresch-Bruneel E, et al: Paclitaxel Given Once Per Week With or Without Bevacizumab in Patients With Advanced Angiosarcoma: A Randomized Phase II Trial, J Clin Oncol. 2015 Sep 1;33(25):2797-802
5. https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Adulte_Weichgewebesarkome/LL_Weichgewebesarkome_Langversion_1.0.pdf

Molecular Diagnostics if clinically resistent to therapy

1. Esperança-Martins M, Melo-Alvim C, Dâmaso S et al. Breast Sarcomas, Phyllodes Tumors, and Desmoid Tumors: Turning the Magnifying Glass on Rare and Aggressive Entities. Cancers (Basel). 2023 Aug 2;15(15):3933.



Metaplastic Breast Carcinoma
- High-Grade -

Consider reference pathology and subtyping.	Oxford LoE	Oxford GR	AGO
▪ Surgical therapy and axillary staging as in case of NST	4	C	++
▪ Neoadjuvant chemotherapy (frequently chemoresistant)*			
▪ If initially inoperable	5	D	+
▪ ER pos.	4	C	--
▪ TNBC, if ICPi (Pembrolizumab) indicated	4	C	+
▪ HER2 pos. (incl. Anti-HER2-therapy)	4	C	+
▪ Adjuvant chemotherapy (frequently chemoresistant)	4	C	-
▪ Consider platin/taxane combination in case of mesenchymal differentiation (e.g. spindle cell)	4	C	+
▪ Adjuvant endocrine therapy if HR-positive	4	C	+
▪ Adjuvant radiotherapy according therapy of NST	4	C	++

* Note: control of local response in short intervals

Therapy review:

1. Corso G, Criscitiello C, Nicosia L et al. Metaplastic breast cancer: an all-round multidisciplinary consensus. Eur J Cancer Prev. 2023 Jul 1;32(4):348-363.
2. Thomas, A., Douglas, E., Reis-Filho, J. S., Gurcan, M. N. & Wen, H. Y. Metaplastic Breast Cancer: Current Understanding and Future Directions. Clin. Breast Cancer (2023)
3. Khoury, T. Metaplastic Breast Carcinoma Revisited; Subtypes Determine Outcomes: Comprehensive Pathologic, Clinical, and Molecular Review. Clin Lab Med 43, 221–243 (2023).
4. Qiu Y, Chen Y, Zhu L, Chen H, Dai Y, Bao B, Tian L, Hao X, Wang J: Differences of Clinicopathological Features between Metaplastic Breast Carcinoma and Nonspecific Invasive Breast Carcinoma and Prognostic Profile of Metaplastic Breast Carcinoma. Breast J 2022;2022:2500594.
5. Khoury T: Metaplastic Breast Carcinoma Revisited; Subtypes Determine Outcomes: Comprehensive Pathologic, Clinical, and Molecular Review. Surg Pathol Clin 2022;15:159–174.
6. Corso G, D'Ecclesiis O, Magnoni F, Mazzotta E, Conforti F, Veronesi P, Sajjadi E, Venetis K, Fusco N, Gandini S: Metaplastic breast cancers and triple-negative breast cancers of no special type: are they prognostically different? A systematic review and meta-analysis. Eur J Cancer Prev 2022;31:459–466.
7. Ong CT, Campbell BM, Thomas SM, Greenup RA, Plichta JK, Rosenberger LH, Force J, Hall A, Hyslop T, Hwang ES, Fayanju OM.

Metaplastic Breast Cancer Treatment and Outcomes in 2500 Patients: A Retrospective Analysis of a National Oncology Database. Ann Surg Oncol. 2018 Aug;25(8):2249–2260. PMCID: PMC6039971

Surgery

1. Pezzi CM, Patel-Parekh L, Cole K, et al (2007). Characteristics and treatment of metaplastic breast cancer: analysis of 892 cases from the National Cancer Data Base. Ann Surg Oncol, 14, 166-73.
2. Harris CG, Azimi F, Chan B, et al. Breast conservation versus mastectomy for metaplastic breast cancer: A systematic review and meta-analysis. Asia Pac J Clin Oncol. 2024 May 29. doi: 10.1111/ajco.14089. Epub ahead of print. PMID: 38808740.

Axilla

1. Murphy BL, Fazzio RT, Hoskin TL, Glazebrook KN, Keeney MG, Habermann EB, Hieken TJ. Management of the axilla in metaplastic breast carcinoma. Gland Surg. 2018 Apr;7(2):200–206. PMCID: PMC5938275

Adjuvant chemotherapy

1. Tzanninis I-G, Kotteas EA, Ntanasis-Stathopoulos I, et al. Management and Outcomes in Metaplastic Breast Cancer. Clinical breast cancer. 2016 Dec;16(6):437–443. PMID: 27431460
2. Drekolias D, Mamounas EP. Metaplastic breast carcinoma: Current therapeutic approaches and novel targeted therapies. Breast Journal. 2019 Nov;25(6):1192–1197. PMID: 31250492
3. Adams S. Dramatic response of metaplastic breast cancer to chemo-immunotherapy. npj Breast Cancer. Nature Publishing Group; 2017;3(1):8–4. PMCID: PMC5445614
4. Lan T, Lu Y, Zheng R, et al. The Role of Adjuvant Chemotherapy in Metaplastic Breast Carcinoma: A Competing Risk Analysis of the SEER Database. Front Oncol. 2021 Apr 26;11:572230. doi: 10.3389/fonc.2021.572230.
5. Corso G, Frassoni S, Girardi A, et al. Metaplastic breast cancer: Prognostic and therapeutic considerations. J Surg Oncol. 2021;123(1):61-70. doi:10.1002/jso.26248
6. Kennedy WR, Gabani P, Acharya S, et al. Clinical outcomes and patterns of care in the treatment of carcinosarcoma of the breast. Cancer Med. 2019 Apr;8(4):1379-1388. (Comment: n=329 (diagnoses 2004-2012, NCDB database), retrospective, med F/U 40m; type of chemotherapy delivered, no data)
7. Xiao M, Yang Z, Tang X, et al. . Clinicopathological characteristics and prognosis of metaplastic carcinoma of the breast. Oncol Lett. 2017 Aug;14(2):1971-1978. (Comment: contradictory results (no DFS benefit, but OS benefit, no effect of RT; subtypes not

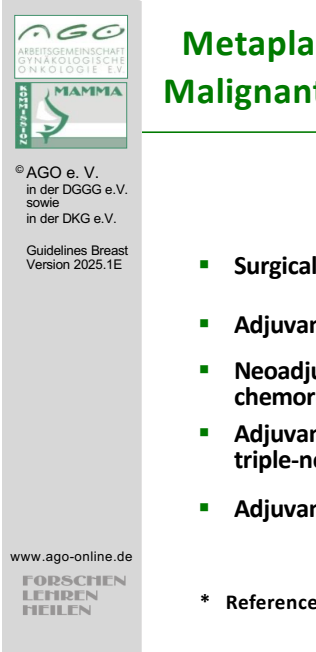
evaluated)
8. Aydiner A, Sen F, Tambas M et al. Metaplastic Breast Carcinoma Versus Triple-Negative Breast Cancer: Survival and Response to Treatment. Medicine (Baltimore). 2015 Dec;94(52):e2341. (Comment: no subtyping (SCC vs mesenchymal, Kontrollgruppe ohne Chemotherapie: 7% (4/54))

Neoadjuvant chemotherapy
1. Al-Hilli Z, Choong G, Keeney MG, et al. Metaplastic breast cancer has a poor response to neoadjuvant systemic therapy. Breast Cancer Res Treat. Springer US; 2019 Aug;176(3):709–716. PMCID: PMC7469521
2. Han M, Salamat A, Zhu L, Zhang H, Clark BZ, Dabbs DJ, Carter GJ, Brufsky AM, Jankowitz RC, Puhalla SL, Johnson RR, Soran A, Steiman JG, McAuliffe PF, Diego EJ, Bhargava R. Metaplastic breast carcinoma: a clinical-pathologic study of 97 cases with subset analysis of response to neoadjuvant chemotherapy. Mod Pathol. Nature Publishing Group; 2019 Jun;32(6):807–816. PMID: 30723293
3. Wong W, Brogi E, Reis-Filho JS, et al. Poor response to neoadjuvant chemotherapy in metaplastic breast carcinoma. NPJ Breast Cancer. 2021 Jul 22;7(1):96. doi: 10.1038/s41523-021-00302-z.
4. Ladipo OL, Ren Y, Caddell KB, et al. Does treatment sequence affect outcomes in patients with metaplastic breast cancer? Am J Surg. 2021 Apr;221(4):701-705. doi: 10.1016/j.amjsurg.2021.01.007. Epub 2021 Jan 18.

Adjuvant endocrine therapy
1. Tzanninis I-G, Kotteas EA, Ntanasis-Stathopoulos I, et al. Management and Outcomes in Metaplastic Breast Cancer. Clinical breast cancer. 2016 Dec;16(6):437–443. PMID: 27431460
2. Paul Wright G, Davis AT, Koehler TJ, et al. Hormone receptor status does not affect prognosis in metaplastic breast cancer: a population-based analysis with comparison to infiltrating ductal and lobular carcinomas. Ann Surg Oncol. 2014 Oct;21(11):3497–3503. PMID: 24838367

Adjuvant radiotherapy
1. Haque W, Verma V, Butler EB, Teh BS. Omission of radiotherapy in elderly women with early stage metaplastic breast cancer. Breast. 2018 Apr;38:154–159. PMID: 29413402
2. Tseng WH, Martinez SR. Metaplastic breast cancer: to radiate or not to radiate? Ann Surg Oncol. 2011 Jan;18(1):94–103. PMCID: PMC3018259
3. Haque W, Verma V, Naik N, et al. Metaplastic Breast Cancer: Practice Patterns, Outcomes, and the Role of Radiotherapy. Ann Surg

Oncol. Springer International Publishing; 2018 Apr;25(4):928–936. PMID: 29322287



Metaplastic Breast Carcinoma – Low Grade With Uncertain Malignant Potential (Fibromatous and Adenosquamous Ca.)*

	Oxford		
	LoE	GR	AGO
▪ Surgical therapy and axillary staging as in case of NST	4	C	++
▪ Adjuvant chemotherapy (frequently chemoresistant)	4	C	-
▪ Neoadjuvant chemotherapy (frequently chemoresistant)	4	C	--
▪ Adjuvant endocrine therapy (not applicable, since triple-negative tumors)	4	C	-
▪ Adjuvant radiotherapy according therapy of NST	4	C	+

* Reference pathology recommended

Review

1. Corso G, Criscitiello C, Nicosia L et al. Metaplastic breast cancer: an all-round multidisciplinary consensus. Eur J Cancer Prev. 2023 Jul 1;32(4):348-363.
2. Thomas, A., Douglas, E., Reis-Filho, J. S., Gurcan, M. N. & Wen, H. Y. Metaplastic Breast Cancer: Current Understanding and Future Directions. Clin. Breast Cancer (2023)
3. Khoury, T. Metaplastic Breast Carcinoma Revisited; Subtypes Determine Outcomes: Comprehensive Pathologic, Clinical, and Molecular Review. Clin Lab Med 43, 221–243 (2023).

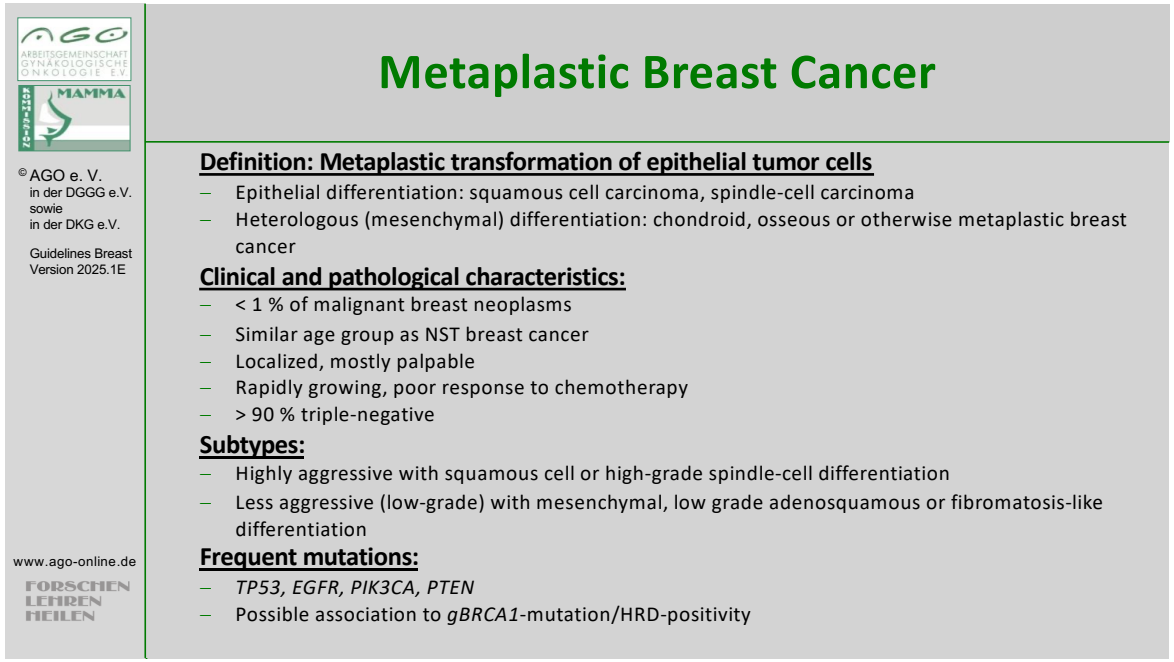
Fibromatose-ähnliches Mammakarzinom (low-grade)

1. Lewis, G. et al. Low-grade adenosquamous carcinoma of the breast: a clinical, morphological and immunohistochemical analysis of 25 patients. Histopathology (2023)
2. Dwyer JB, Clark BZ. Low-grade fibromatosis-like spindle cell carcinoma of the breast. Arch Pathol Lab Med. 2015 Apr;139(4):552–557. PMID: 25822766
3. Nonnis R, Paliogiannis P, Giangrande D, Marras V, Trignano M. Low-grade fibromatosis-like spindle cell metaplastic carcinoma of the breast: a case report and literature review. Clinical breast cancer. 2012 Apr;12(2):147–150. PMID: 22444721
4. Barnes PJ, Boutilier R, Chiasson D, Rayson D. Metaplastic breast carcinoma: clinical-pathologic characteristics and HER2/neu

expression. Breast Cancer Res Treat. 2005;91(2):173-178. doi:10.1007/s10549-004-7260-y.
5. Sneige N, Yaziji H, Mandavilli SR, Perez ER, Ordonez NG, Gown AM, Ayala A. Low-grade (fibromatosis-like) spindle cell carcinoma of the breast. The American journal of surgical pathology. 2001 Aug;25(8):1009–1016. PMID: 11474284
6. Russell DH, Montgomery EA, Susnik B. Low to Intermediate (Borderline) Grade Breast Spindle Cell Lesions on Needle Biopsy: Diagnostic Approach and Clinical Management. Adv Anat Pathol. 2022 Sep 1;29(5):309-323. doi: 10.1097/PAP.0000000000000353. Epub 2022 Jul 12. PMID: 35838633.

Adenosquamöses metaplastisches Karzinom (low grade)

1. Soo K, Tan PH. Low-grade adenosquamous carcinoma of the breast. J Clin Pathol. 2013 Jun;66(6):506–511. PMID: 23268316
2. Wilsher MJ. Adenosquamous proliferation of the breast and low grade adenosquamous carcinoma: a common precursor of an uncommon cancer? Pathology. 2014 Aug;46(5):402–410. PMID: 24842378
3. Kanthan R, Senger JL. Low-Grade Adenosquamous Carcinoma [LGASC] of the Breast and Syringomatous Adenoma of the Nipple [SAN]: A Single Entity with Two Homes? SciMed Central. BMJ Publishing Group; 2014;2(3):1026.
4. Romanucci G, Mercogliano S, Carucci Eet al. Low-grade adenosquamous carcinoma of the breast: a review with focus on imaging and management. Acta Radiol Open. 2021 Apr 30;10(4):20584601211013501. doi: 10.1177/20584601211013501.
5. Cserni G, Quinn CM, Foschini MP, et al, European Working Group For Breast Screening Pathology. Triple-Negative Breast Cancer Histological Subtypes with a Favourable Prognosis. Cancers (Basel). 2021 Nov 14;13(22):5694. doi: 10.3390/cancers13225694.



Background

1. Qiu Y, Chen Y, Zhu L, et al.: Differences of Clinicopathological Features between Metaplastic Breast Carcinoma and Nonspecific Invasive Breast Carcinoma and Prognostic Profile of Metaplastic Breast Carcinoma. Breast J 2022;2022:2500594.
2. WHO. Breast Tumours: WHO Classification of Tumours. 5 ed. Lyon (France): International Agency for Research on Cancer; 2019.
3. McCart Reed AE, Kalaw E, Nones K, et al. Phenotypic and molecular dissection of metaplastic breast cancer and the prognostic implications. J Pathol. 2019 Feb;247(2):214–227. PMID: 30350370
4. Rakha EA, Coimbra NDM, Hodi Z, et al. Immunoprofile of metaplastic carcinomas of the breast. Histopathology. 2017 May;70(6):975–985. PMID: 28029685
5. Leyrer CM, Berriochoa CA, Agrawal S, et al. Predictive factors on outcomes in metaplastic breast cancer. Breast Cancer Res Treat. 3rd ed. Springer US; 2017 Oct;165(3):499–504. PMID: 28689362
6. Budzik MP, Patera J, Sobol M, et al. characteristics of metaplastic breast cancer - analysis of the basic immunohistochemical profile and comparison with other invasive breast cancer types. Breast. 2019 Feb;43:135–141. PMID: 30553188
7. Corso G, Frassoni S, Girardi A, et al. Metaplastic breast cancer: Prognostic and therapeutic considerations. J Surg Oncol. 2021 Jan;123(1):61-70. doi: 10.1002/jso.26248. Epub 2020 Oct 12. PMID: 33047318.

Outcome

1. Corso G, D'Ecclesiis O, Magnoni F, et al: Metaplastic breast cancers and triple-negative breast cancers of no special type: are they prognostically different? A systematic review and meta-analysis. Eur J Cancer Prev 2022;31:459–466.
2. Khoury T: Metaplastic Breast Carcinoma Revisited; Subtypes Determine Outcomes: Comprehensive Pathologic, Clinical, and Molecular Review. Surg Pathol Clin 2022;15:159–174.
3. Tadros AB, Sevilimedu V, Giri DD, et al. Survival Outcomes for Metaplastic Breast Cancer Differ by Histologic Subtype. Ann Surg Oncol. Springer International Publishing; 2021 Jan 2;23:481–9. PMID: 33389291
4. Polamraju P, Haque W, Cao K, et al. Comparison of outcomes between metaplastic and triple-negative breast cancer patients. Breast. 2020 Feb;49:8–16. PMCID: PMC7375639
5. Li Y, Zhang N, Zhang H, Yang Q. Comparative prognostic analysis for triple-negative breast cancer with metaplastic and invasive ductal carcinoma. J Clin Pathol. BMJ Publishing Group; 2019 Jun;72(6):418–424. PMID: 30872384
6. He X, Ji J, Dong R, Liu H, et al. Prognosis in different subtypes of metaplastic breast cancer: a population-based analysis. Breast Cancer Res Treat. Springer US; 2019 Jan;173(2):329–341. PMID: 30341462
7. Leyrer CM, Berriochoa CA, Agrawal S, et al. Predictive factors on outcomes in metaplastic breast cancer. Breast Cancer Res Treat. 3rd ed. Springer US; 2017 Oct;165(3):499–504. PMID: 28689362
8. Tadros AB, Sevilimedu V, Giri DD, et al. Survival Outcomes for Metaplastic Breast Cancer Differ by Histologic Subtype. Ann Surg Oncol. 2021 Aug;28(8):4245-4253. doi: 10.1245/s10434-020-09430-5. Epub 2021 Jan 2.
9. Corso G, Frassoni S, Girardi A, et al. Metaplastic breast cancer: Prognostic and therapeutic considerations. J Surg Oncol. 2021 Jan;123(1):61-70. doi: 10.1002/jso.26248. Epub 2020 Oct 12.

Molecular features

1. Tray N, Taff J, Singh B, et al. Metaplastic breast cancers: Genomic profiling, mutational burden and tumor-infiltrating lymphocytes. Breast. 2019 Apr;44:29–32. PMID: 30609392

2. Edenfield J, Schammel C, Collins J, et al. Metaplastic Breast Cancer: Molecular Typing and Identification of Potential Targeted Therapies at a Single Institution. Clinical breast cancer. 2017 Feb;17(1):e1–e10. PMID: 275681017
3. Zhai J, Giannini G, Ewalt MD, et Molecular characterization of metaplastic breast carcinoma via next-generation sequencing. Hum Pathol. 2019 Apr;86:85–92. PMID: 30537493
4. Afkhami M, Schmolze D, Yost SE, et al. Mutation and immune profiling of metaplastic breast cancer: Correlation with survival. PLoS One. 2019 Nov 6;14(11):e0224726. doi: 10.1371/journal.pone.0224726. PMID: 31693690; PMCID: PMC6834262.