Diagnosis and Treatment of Patients with early and advanced Breast Cancer

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Guidelines Breast
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Pathology

Screened data bases: PubMed 2020.

Search Query:

(Breast Diseases/PA[mh] AND ("2010/01/01"[dp] : "2020/01/01"[dp]) AND ("english"[la] OR "german"[la])

Guidelines screened

1. Hoon TP, Ellis I, Allison K, et al. The 2019 WHO classification of tumours of the breast. Histopathology. February 2020. doi:10.1111/his.14091.
2. National Comprehensive Cancer Network (NCCN). Breast Cancer, Version 1.2020, NCCN Clinical Practice Guidelines in Oncology. January 2020:1-223.
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8. The Royal College of Pathologists. Pathology reporting of breast disease in surgical excision specimens incorporating the dataset for histological reporting of breast cancer. June 2016:1-160. https://www.rcpath.org/profession/publications/cancer-datasets.html.
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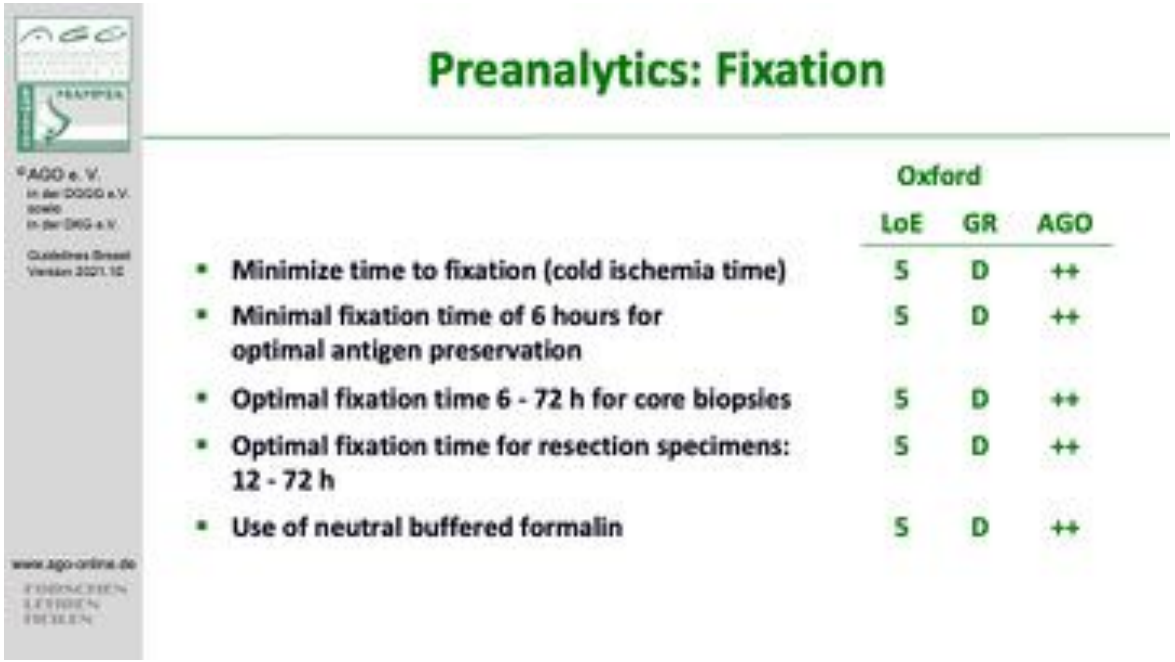

Antigen preservation

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Retraction artifacts

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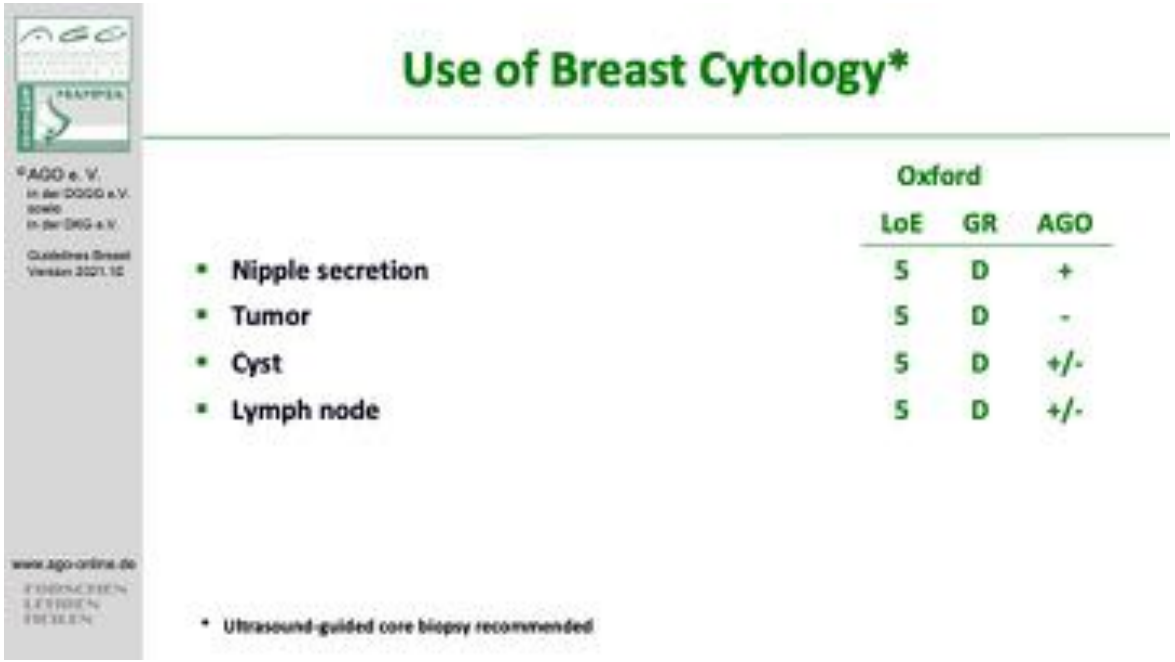
2. Lester, S. C., Bose, S., Chen, Y.-Y., et al. (2009). Protocol for the examination of specimens from patients with invasive carcinoma of the breast. Arch Pathol Lab Med, 133(10), 1515–1538.



1. Day, C, N Moatamed, AM Fimbres, et al: A Retrospective Study of the Diagnostic Accuracy of Fine-Needle Aspiration for Breast Lesions and Implications for Future Use. Diagnostic Cytopathology 36, no. 12 (November 30, 2008): 855–60.
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6. Bruzzone, M., Saro, F., Bruno, S. et al. (2018). Synergy of cytological methods in the pathological staging of breast cancer: Axillary fine-needle aspiration and intraoperative scrape cytology of the sentinel lymph node. Diagnostic Cytopathology, 46(11), 919–926. http://doi.org/10.1002/dc.23995
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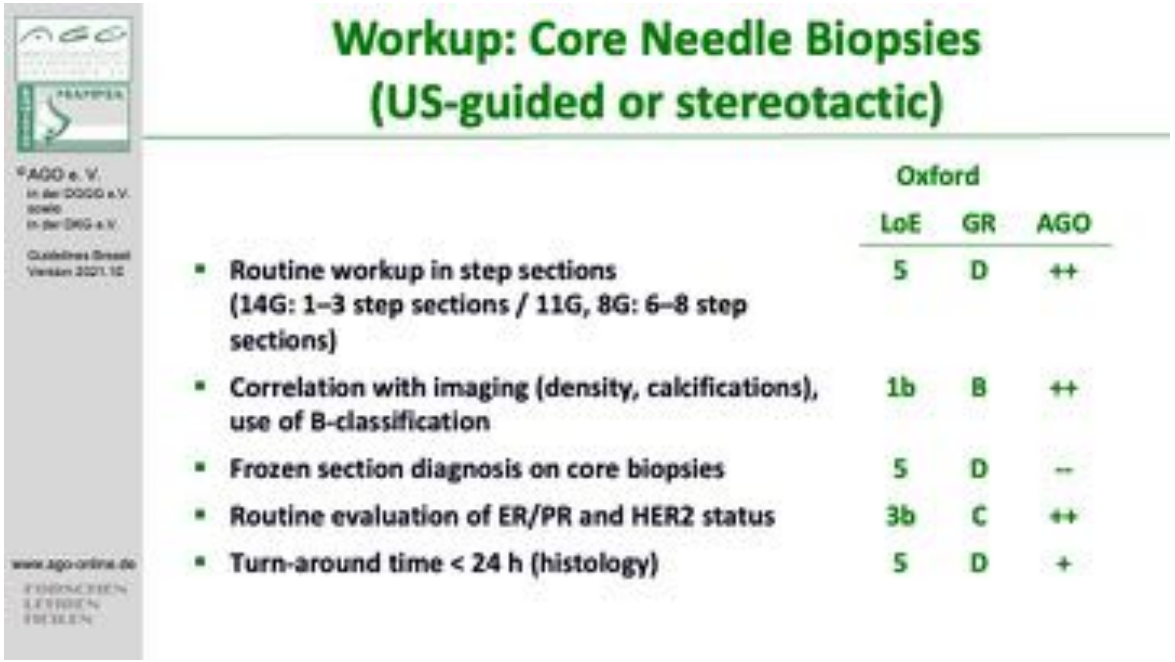

Statement: Routine workup in step sections

1. Hahn, M., Krainick-Strobel, U., Toellner, T. et al. (2012). Interdisciplinary consensus recommendations for the use of vacuum-assisted breast biopsy under sonographic guidance: first update 2012. Ultraschall Med, 33(4), 366–371. http://doi.org/10.1055/s-0032-1312831
2. Sinn, Gerber, Brucker et al. (2017): DCIS und Risikoläsionen. In: AWMF: S3-Leitlinie Früherkennung, Diagnostik, Therapie und Nachsorge des Mammakarzinoms, S. 79 - 89.

Statement: Correlation with imaging

1. Heywang-Köbrunner SH, Sinnatamby R, Lebeau A, et al; Consensus Group. Interdisciplinary consensus on the uses and technique of MR-guided vacuum-assisted breast biopsy (VAB): results of a European consensus meeting. Eur J Radiol. 2009 Nov;72(2):289-94
2. Sinn, Gerber, Brucker et al. (2017): DCIS und Risikoläsionen. In: AWMF: S3-Leitlinie Früherkennung, Diagnostik, Therapie und Nachsorge des Mammakarzinoms, S. 79 - 89.

Statement: Frozen section diagnosis on core biopsies

1. Lebeau, Gerber, Brucker et al. (2017): Pathomorphologische Untersuchung. In: AWMF: S3-Leitlinie Früherkennung, Diagnostik, Therapie und Nachsorge des Mammakarzinoms, S. 100 - 139.
2. Dämmrich, M., Thomssen, C., Hillemanns, P. et al. (2012). Intraoperative pathologische Sofortuntersuchung in der Mammachirurgie. Der Pathologe, 33(5), 424–429. http://doi.org/10.1007/s00292-012-1596-6

Statement: Routine evaluation of ER/PgR and HER-2 status

1. Dekker, T. J. A., Smit, V. T. H. B. M., Hooijer, G. K. J. et al. (2013). Reliability of core needle biopsy for determining ER and HER2 status in breast cancer. Annals of Oncology, 24(4), 931–937. http://doi.org/10.1093/annonc/mds599
2. Meattini, I., Bicchierai, G., Saieva, C. et al. (2017). Impact of molecular subtypes classification concordance between preoperative core needle biopsy and surgical specimen on early breast cancer management: Single-institution experience and review of published literature. European Journal of Surgical Oncology : the Journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology, 43(4), 642–648. http://doi.org/10.1016/j.ejso.2016.10.025

Statement: Turn-around time < 24h

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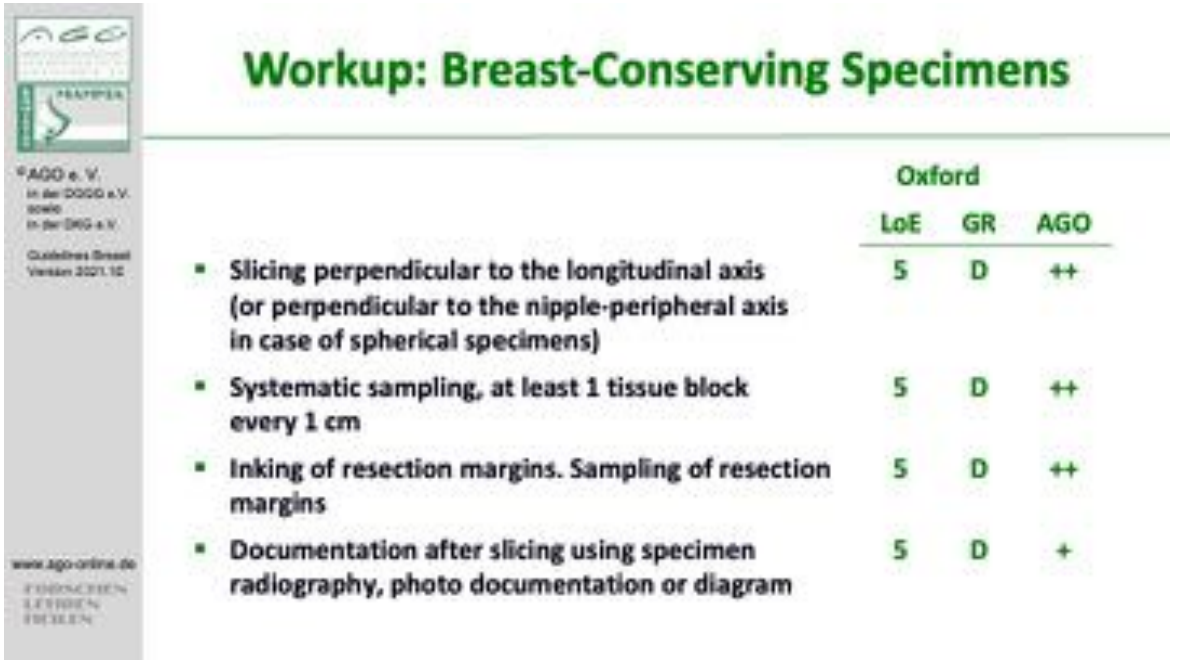

Guidelines

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Systematic Sampling

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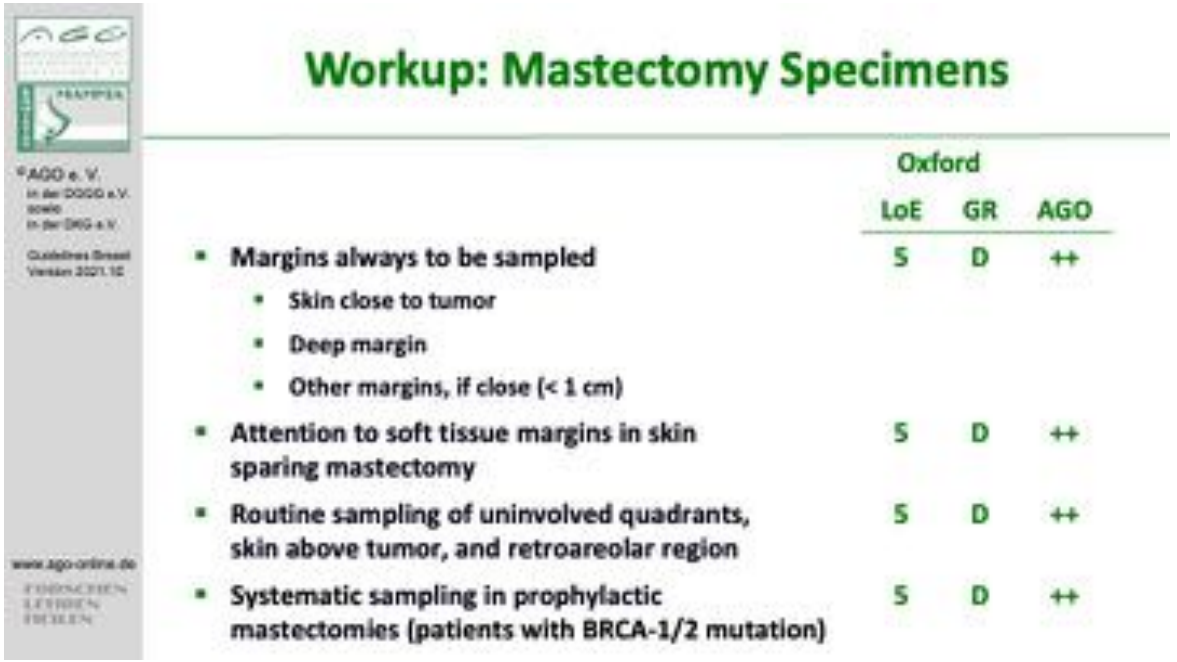

Guidelines

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Skin sparing and nipple sparing mastectomy

1. Papassotiropoulos B, Güth U, Chiesa F, et al. Prospective Evaluation of Residual Breast Tissue After Skin- or Nipple-Sparing Mastectomy: Results of the SKINI-Trial. Ann Surg Oncol. 2019;26(5):1254-1262. doi:10.1245/s10434-019-07259-1.
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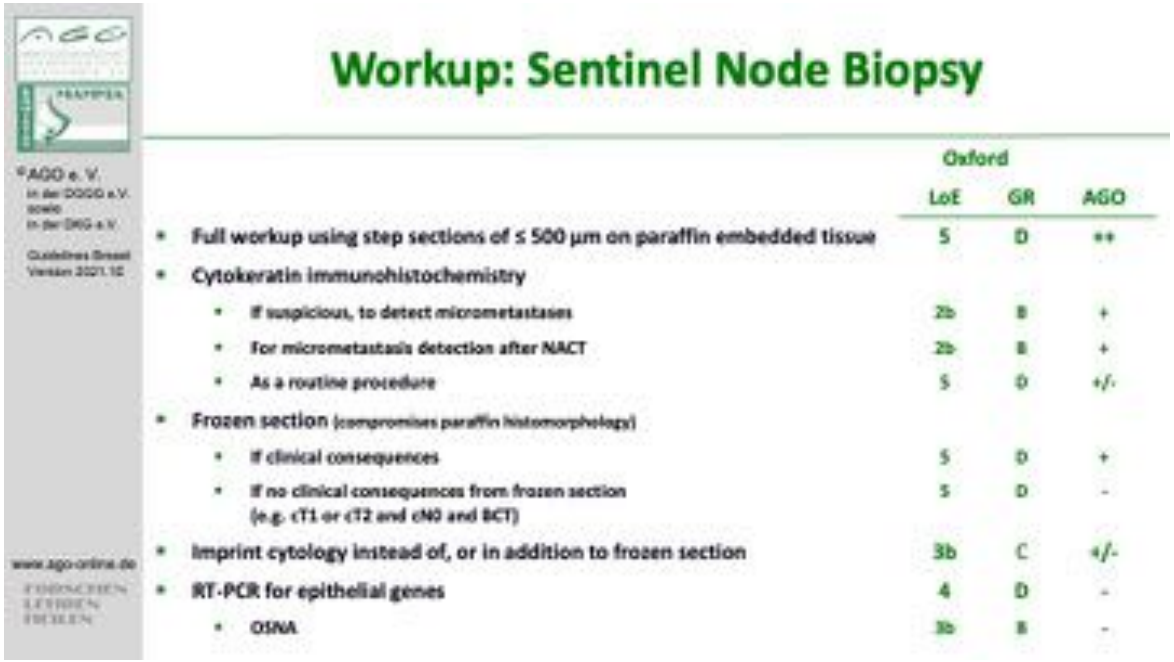


Statement: Evaluation of sentinel node biopsy

1. Maguire, A., & Brogi, E. (2016). Sentinel lymph nodes for breast carcinoma: an update on current practice. *Histopathology*, *68*(1), 152–167. http://doi.org/10.1111/his.12853
2. Liu L-C, Lang JE, Lu Y, et al. Intraoperative frozen section analysis of sentinel lymph nodes in breast cancer patients: a meta-analysis and single-institution experience. *Cancer*. 2011;117(2):250-258. doi:10.1002/cncr.25606.

Statement: Full workup using step sections of ≥ 500 µm on paraffin embedded tissue

1. Maguire, A., & Brogi, E. (2016). Sentinel lymph nodes for breast carcinoma: an update on current practice. *Histopathology*, *68*(1), 152–167. http://doi.org/10.1111/his.12853

Statement: Frozen section

1. Langer, I., Guller, U., Berclaz, G. et al. (2009). Accuracy of frozen section of sentinel lymph nodes: a prospective analysis of 659 breast cancer patients of the Swiss multicenter study. *Breast Cancer Research and Treatment*, *113*(1), 129–136.

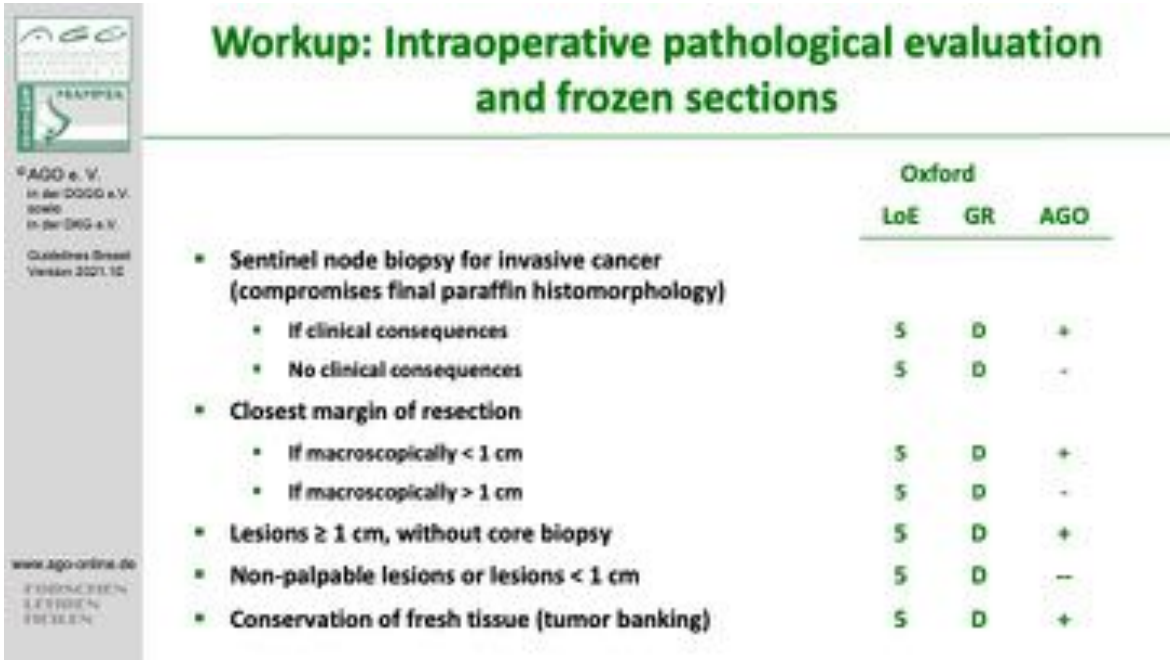
http://doi.org/10.1007/s10549-008-9911-x

Statement: Imprint cytology instead or in addition of frozen section

1. Layfield et al. Intraoperative assessment of sentinel lymph nodes in breast cancer. The British journal of surgery (2011) vol. 98 (1) pp. 4-17
2. Upender, S., Mohan, H., Handa, U. et al. (2009). Intraoperative evaluation of sentinel lymph nodes in breast carcinoma by imprint cytology, frozen section and rapid immunohistochemistry. *Diagnostic Cytopathology*, *37*(12), 871–875. http://doi.org/10.1002/dc.21120

Statement: RT-PCR for epithelial genes

1. Layfield, D. M., Agrawal, A., Roche, H. et al. (2011). Intraoperative assessment of sentinel lymph nodes in breast cancer. *The British Journal of Surgery*, *98*(1), 4–17. http://doi.org/10.1002/bjs.7229
2. Visser, M., Jiwa, M., Horstman, A. et al. (2008). Intra-operative rapid diagnostic method based on CK19 mRNA expression for the detection of lymph node metastases in breast cancer. *International Journal of Cancer Journal International Du Cancer*, *122*(11), 2562–2567. http://doi.org/10.1002/ijc.23451



Statement: Sentinel node biopsy for invasive cancer

1. Kühn T, Bembenek A, Decker T et al. A concept for the clinical implementation of sentinel lymph node biopsy in patients with breast carcinoma with special regard to quality assurance. Cancer 2005; 103: 451-461.
2. Grabau D, Rank F, Friis E. Intraoperative frozen section examination of axillary sentinel lymph nodes in breast cancer. APMIS 2005; 113: 7-12.
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Statement: Closest margin of resection

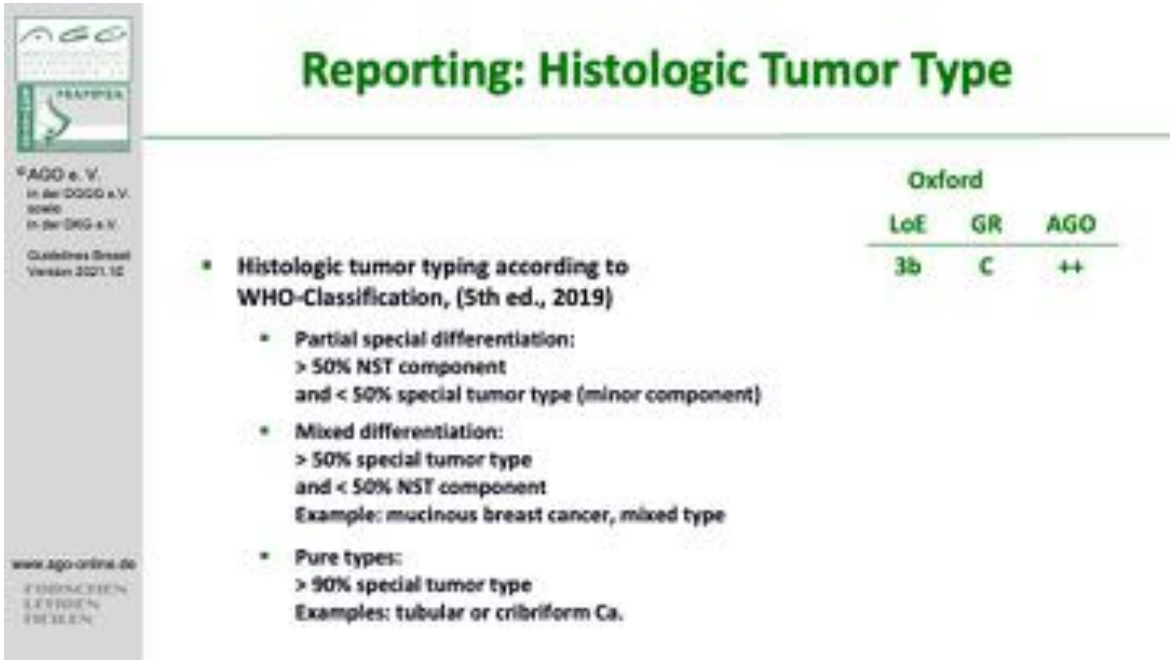
1. Reiner-Concin A, Lax S. Mammakarzinom. In: Manual der gynäkologischen Onkologie (Reinthaler R, Helfer L, Hrsg.). http://www.ago-manual.at/inhalt/i-mammakarzinom/15-pathologie/
2. Kraus-Tiefenbacher U, Scheda A, Steil V, et al.Intraoperative radiotherapy (IORT) for breast cancer using the Intrabeam system. Tumori. 2005;91:339-45

Statement: Lesions ≥ 1 cm, without core biopsy

1. Reiner-Concin A, Lax S. Mammakarzinom. In: Manual der gynäkologischen Onkologie (Reinthaler R, Helfer L, Hrsg.). http://www.ago-manual.at/inhalt/i-mammakarzinom/15-pathologie/
2. Fitzgibbons PL, Connolly JL, Page DL. Updated protocol for the examination of specimens from patients with carcinomas of the breast. Arch Pathol Lab Med 2000; 124:1026- 1033. (ACR)
3. Amendoeira I, Apostolikas N, Bellocq et al. Quality assurance guidelines for pathology: Open biopsy and resection specimens. In: Perry N, Broders M, de Wolf C, et al (eds) European guidelines for quality assurance in breast cancer screening and diagnosis; Office for Official Publications of the European Communities, Luxembourg, 2006, pp 256-311

Statement: Non-palpable lesions or lesions < 1 cm

1. Morrow M, Strom E, Bassett L et al. Standard for the management of ductal carcinoma in situ of the breast (DCIS). CA Cancer J Clin 2002; 52: 256-276.



WHO-Classification

1. Hoon TP, Ellis I, Allison K, et al. The 2019 WHO classification of tumours of the breast. *Histopathology*. February 2020. doi:10.1111/his.14091.
2. WHO. Breast Tumours: WHO Classification of Tumours. 5 ed. Lyon (France): International Agency for Research on Cancer; 2019.
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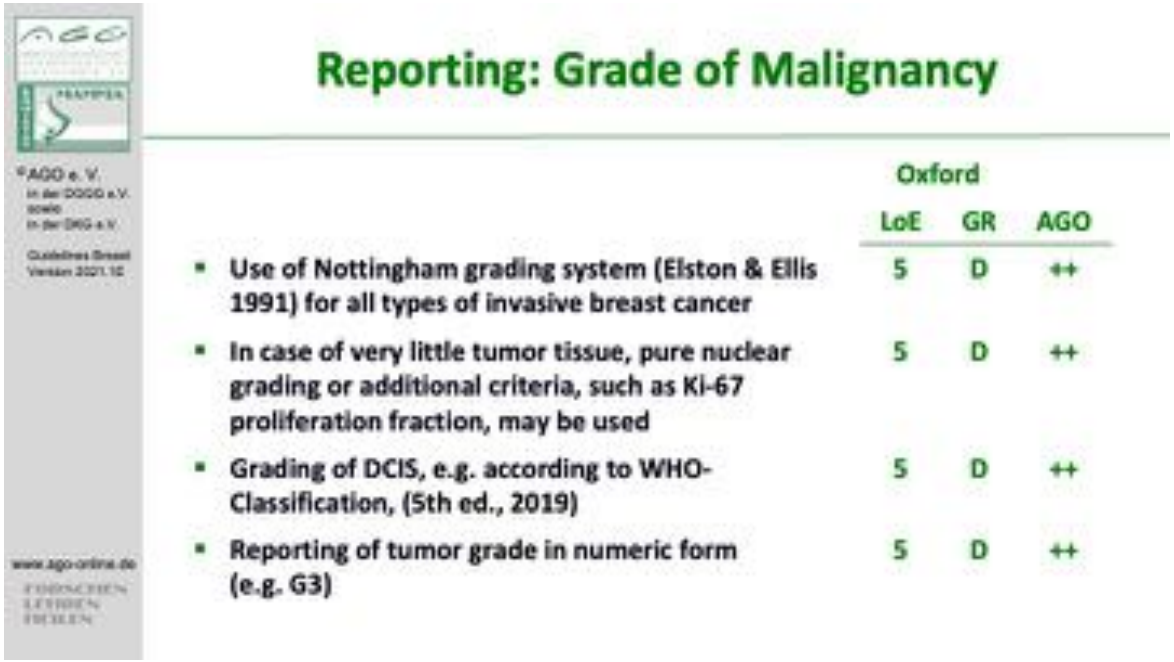

Grading

1. Elston C, Ellis I. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. *Histopathology*. 1991;19(5):403-41
2. WHO. Breast Tumours: WHO Classification of Tumours. 5 ed. Lyon (France): International Agency for Research on Cancer; 2019
3. Christgen M, Länger F, Kreipe H. Histologisches Grading beim Mammakarzinom. *Der Pathologe*. 2016;37(4):328-336. doi:10.1007/s00292-016-0182-8.
4. Chang JM, McCullough AE, Dueck AC, et al. Back to Basics: Traditional Nottingham Grade Mitotic Counts Alone are Significant in Predicting Survival in Invasive Breast Carcinoma. *Ann Surg Oncol*. 2015;22 Suppl 3:S509-S515. doi:10.1245/s10434-015-4616-y.
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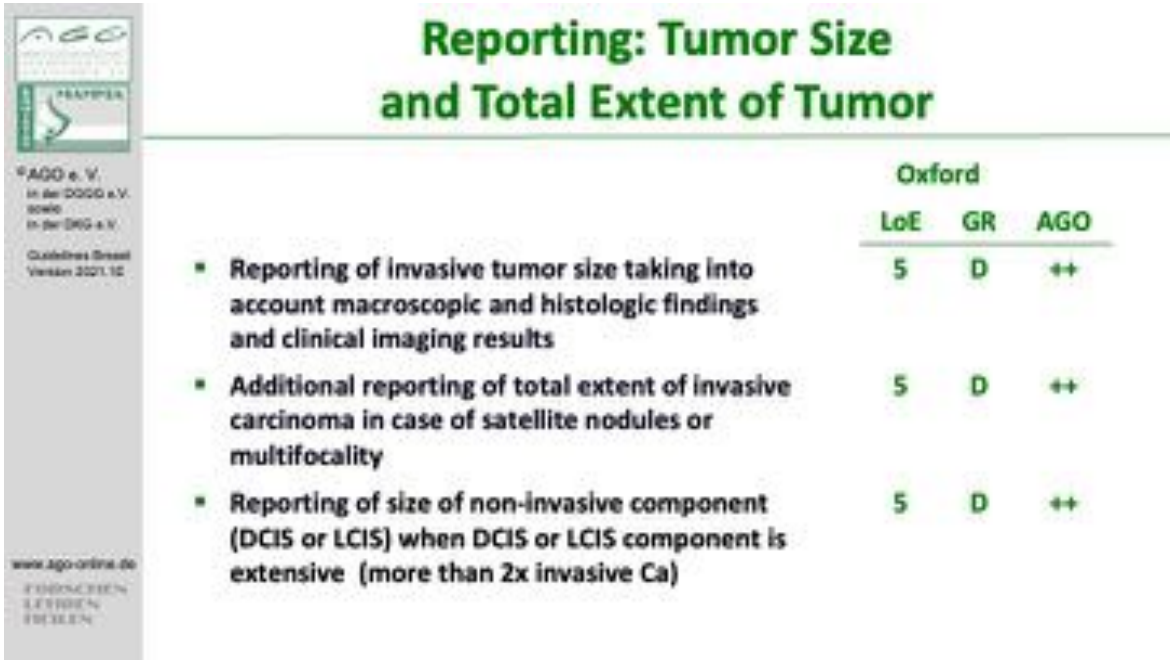

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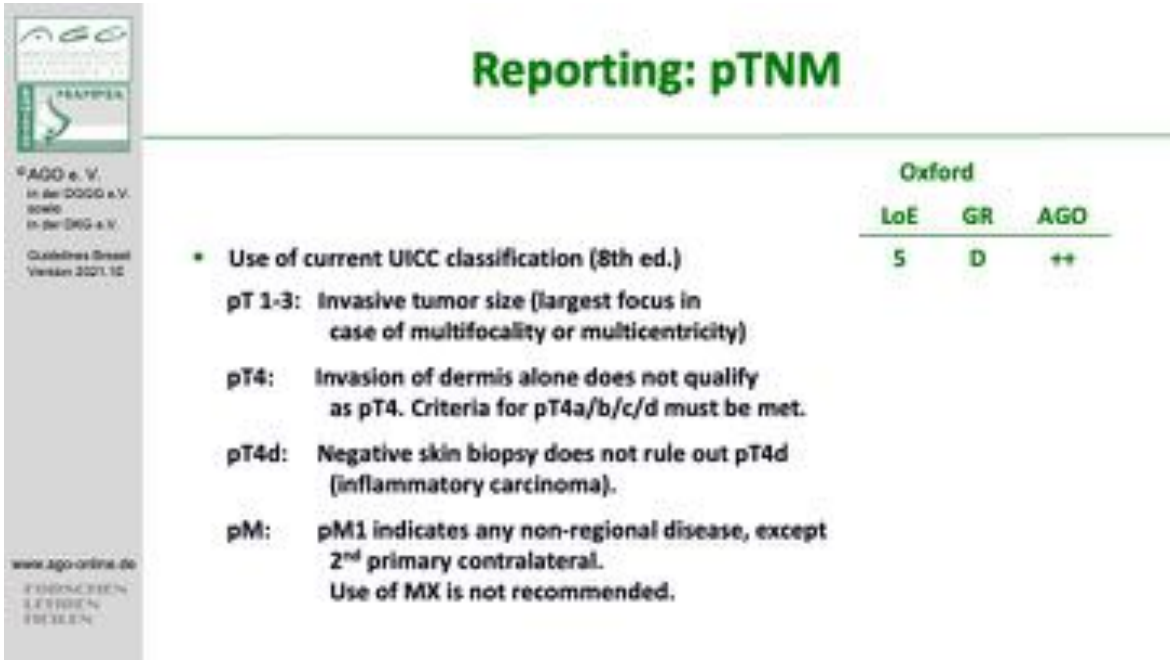

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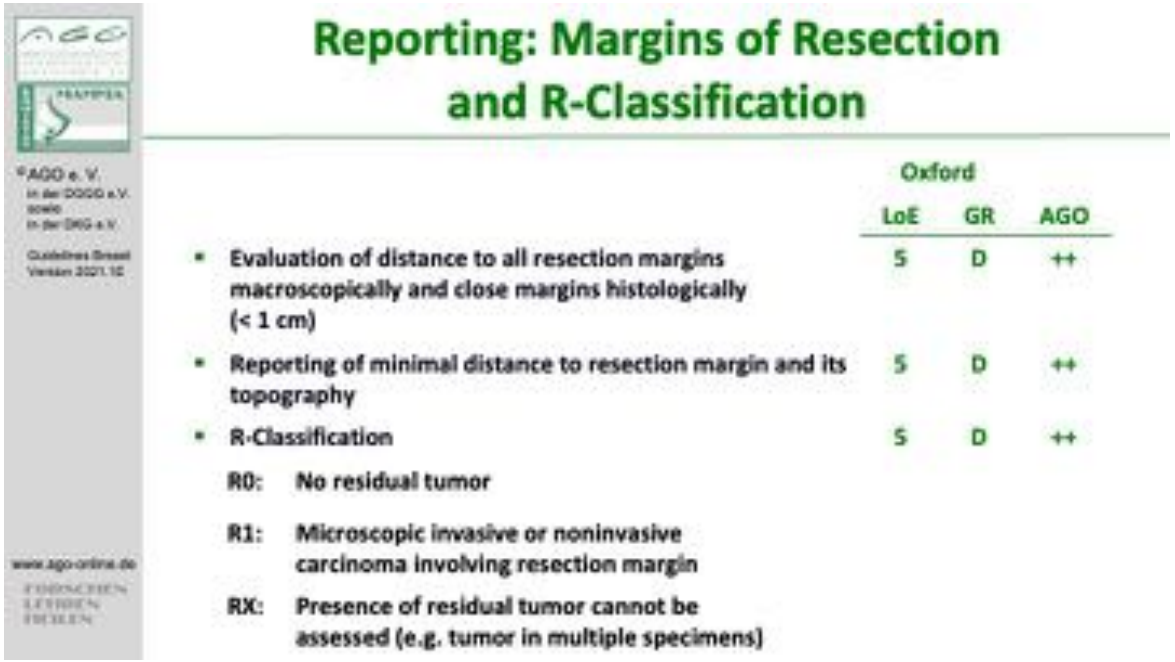

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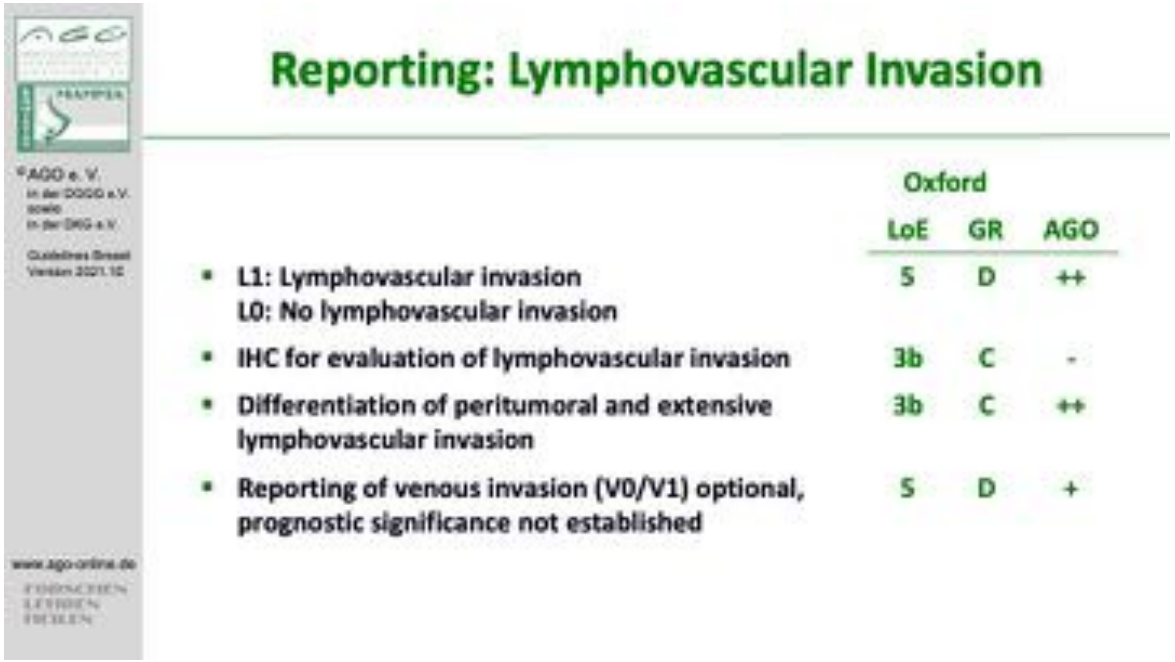

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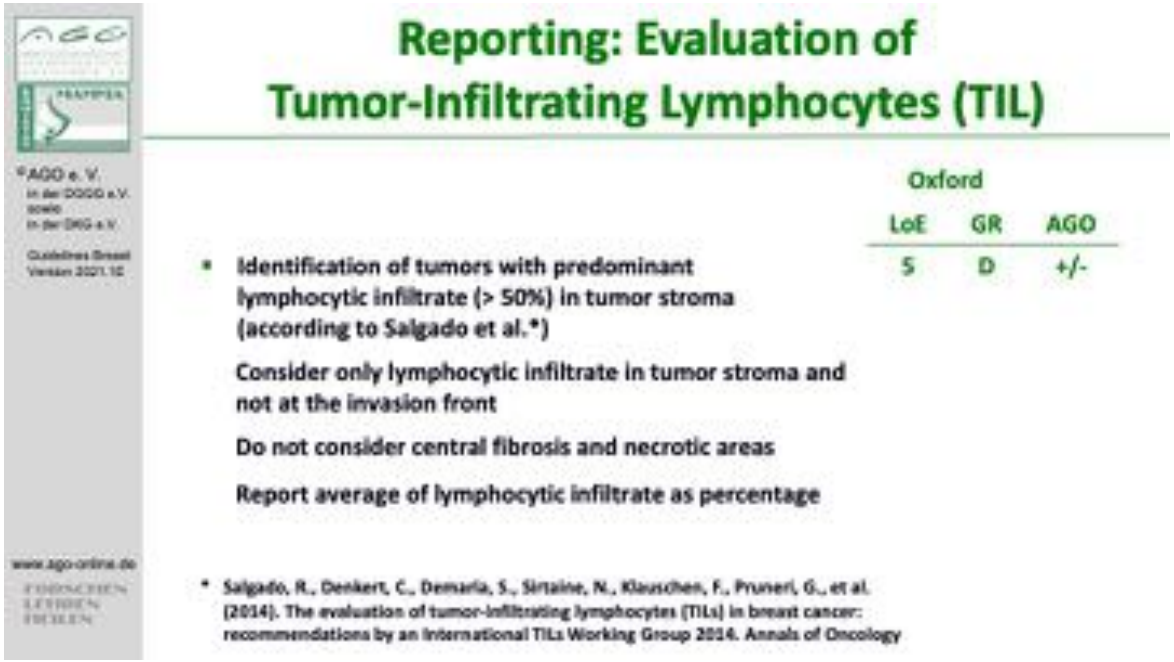

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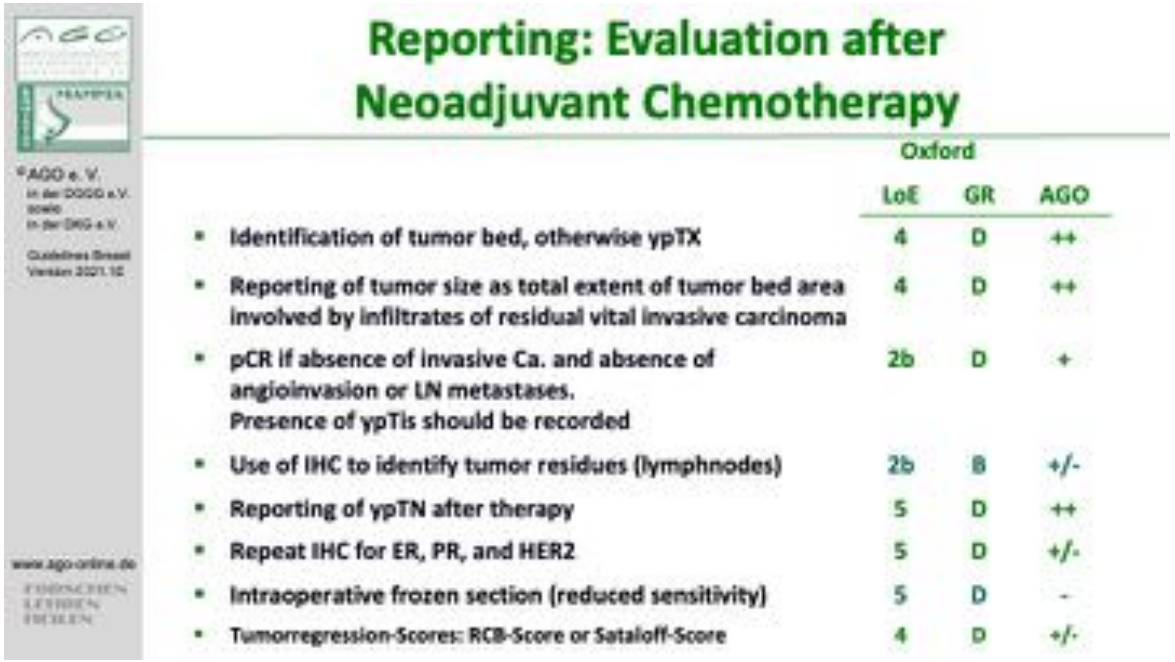

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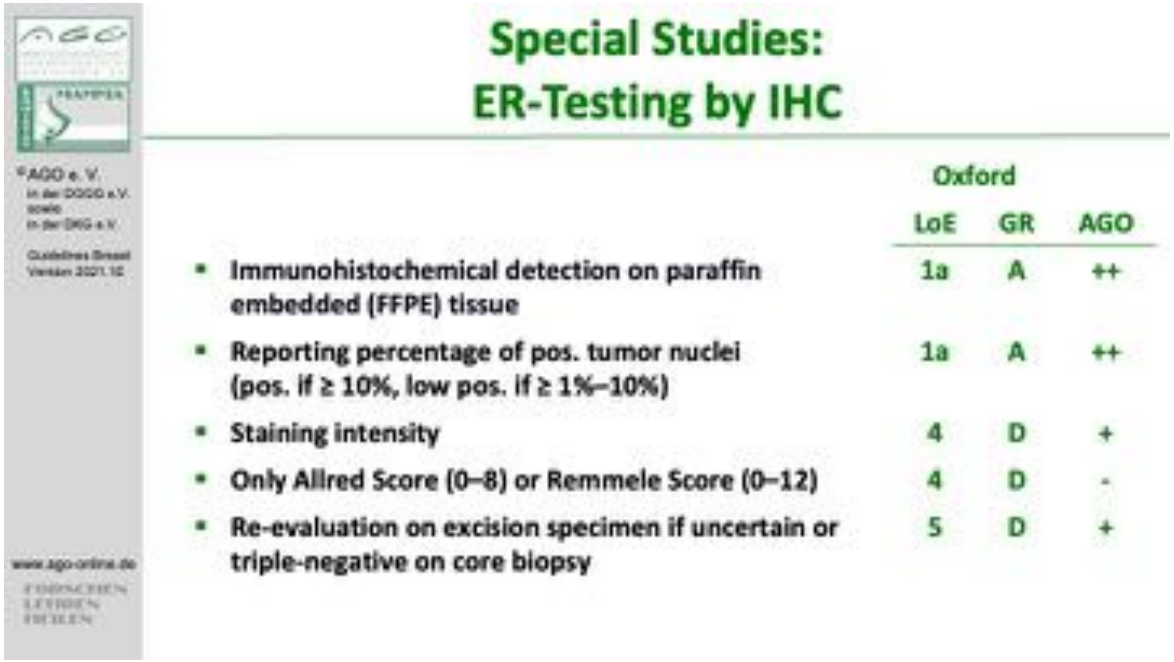

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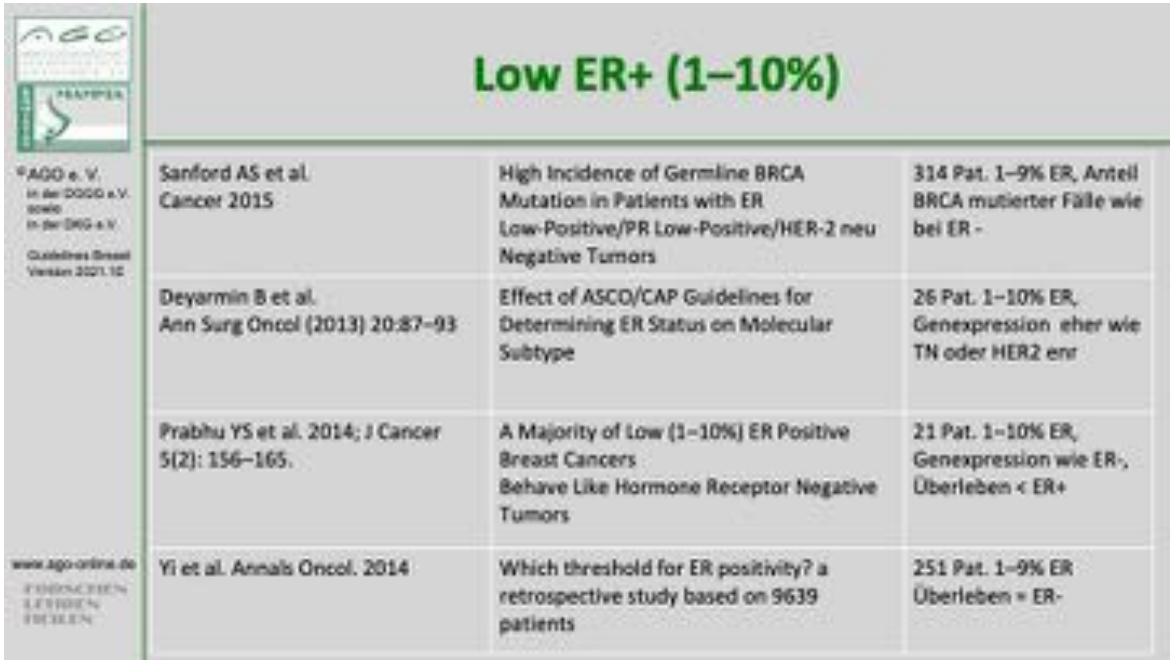

Low ER+ (1–10%)

Sanford AS et al. Cancer 2015	High Incidence of Germline BRCA Mutation in Patients with ER Low-Positive/PR Low-Positive/HER-2 neu Negative Tumors	314 Pat. 1–9% ER, Anteil BRCA mutierter Fälle wie bei ER -
Deyarmin B et al. Ann Surg Oncol (2013) 20:87–93	Effect of ASCO/CAP Guidelines for Determining ER Status on Molecular Subtype	26 Pat. 1–10% ER, Genexpression eher wie TN oder HER2 enr
Prabhu YS et al. 2014; J Cancer 5(2): 156–165.	A Majority of Low (1–10%) ER Positive Breast Cancers Behave Like Hormone Receptor Negative Tumors	21 Pat. 1–10% ER, Genexpression wie ER-, Überleben < ER+
Yi et al. Annals Oncol. 2014	Which threshold for ER positivity? a retrospective study based on 9639 patients	251 Pat. 1–9% ER Überleben = ER-

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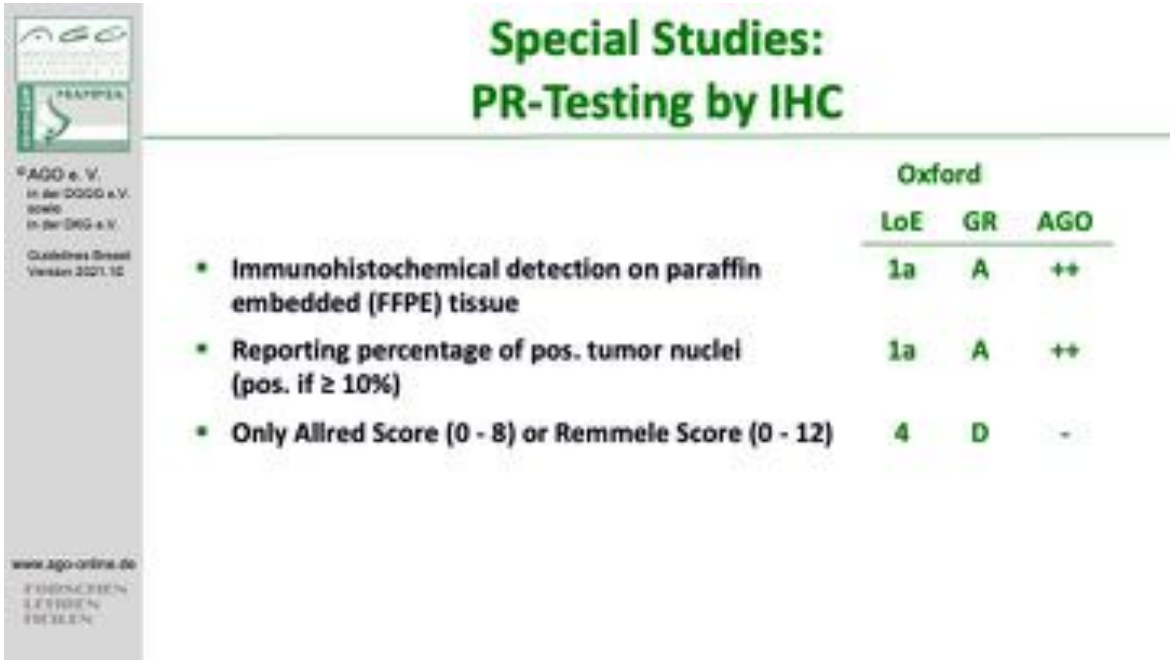

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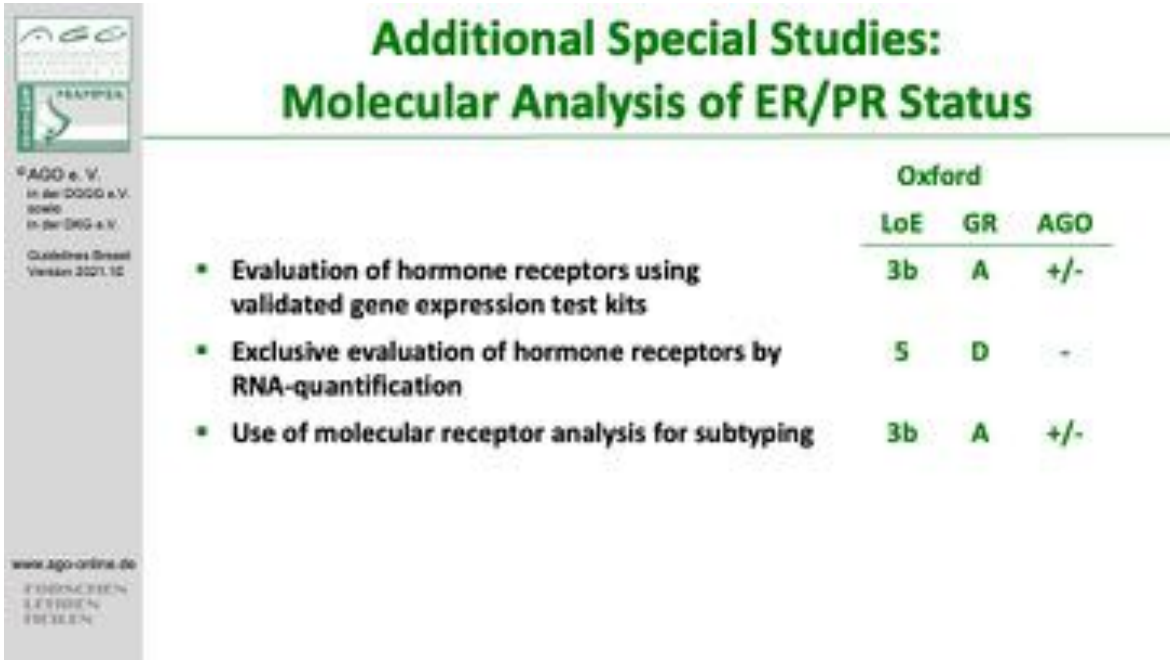

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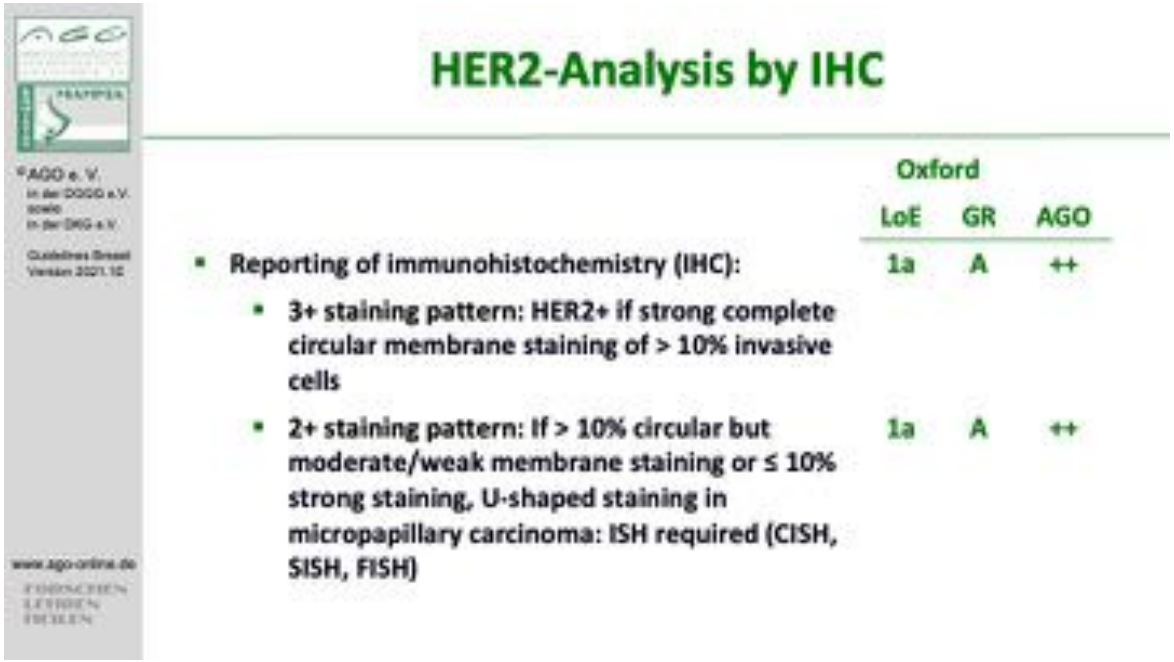

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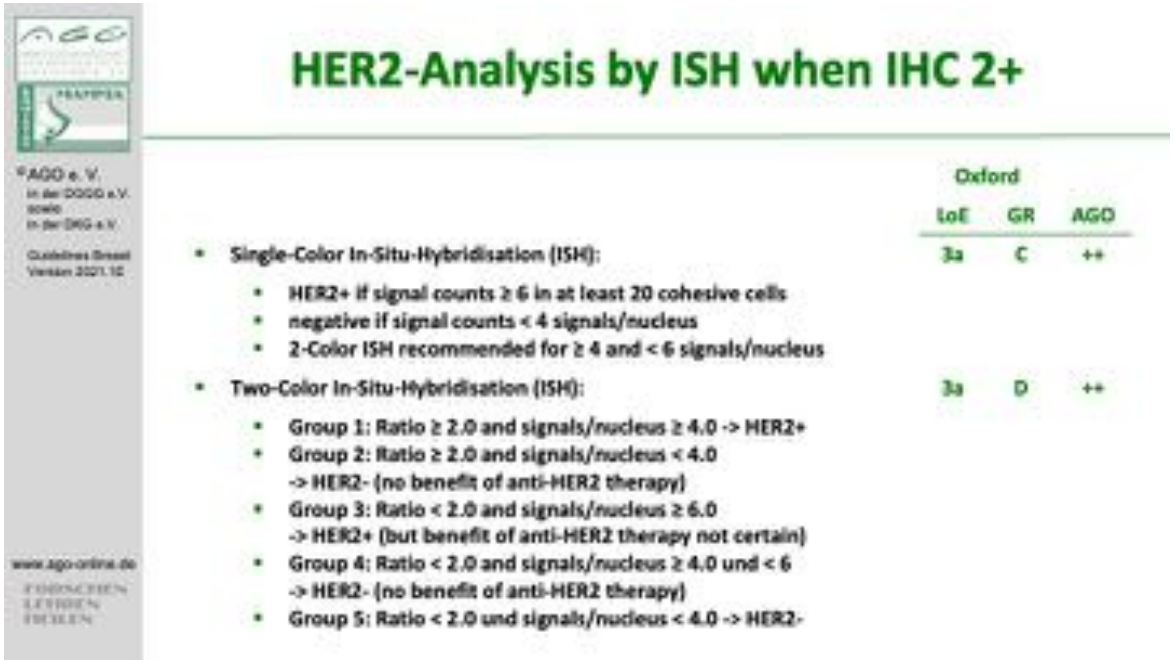

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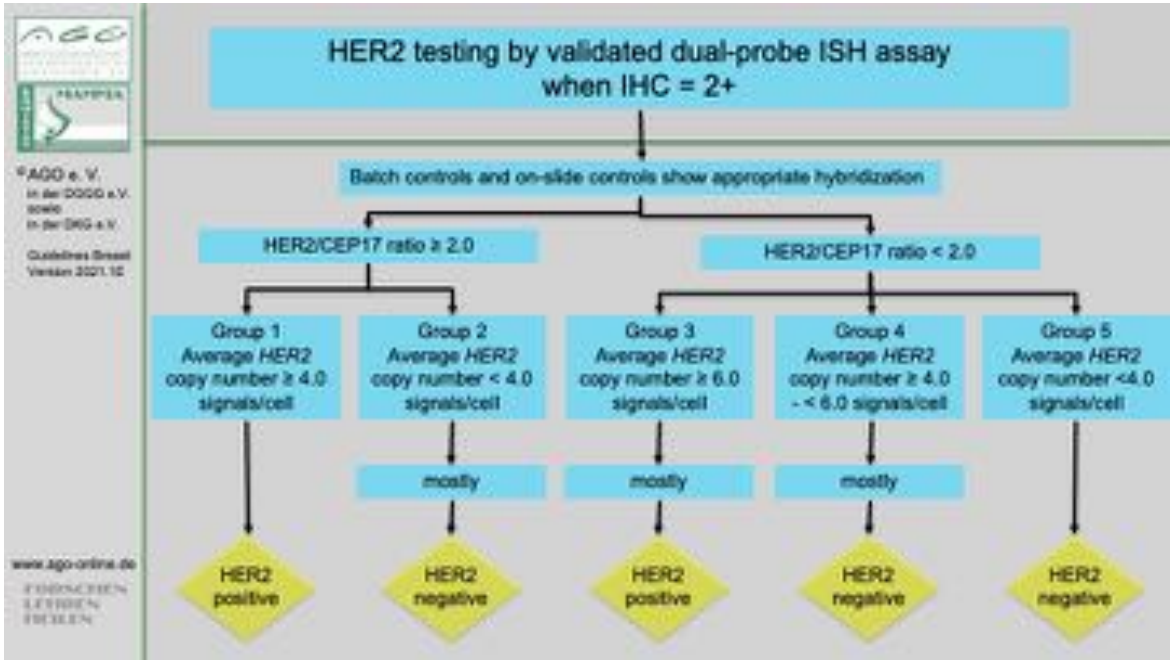

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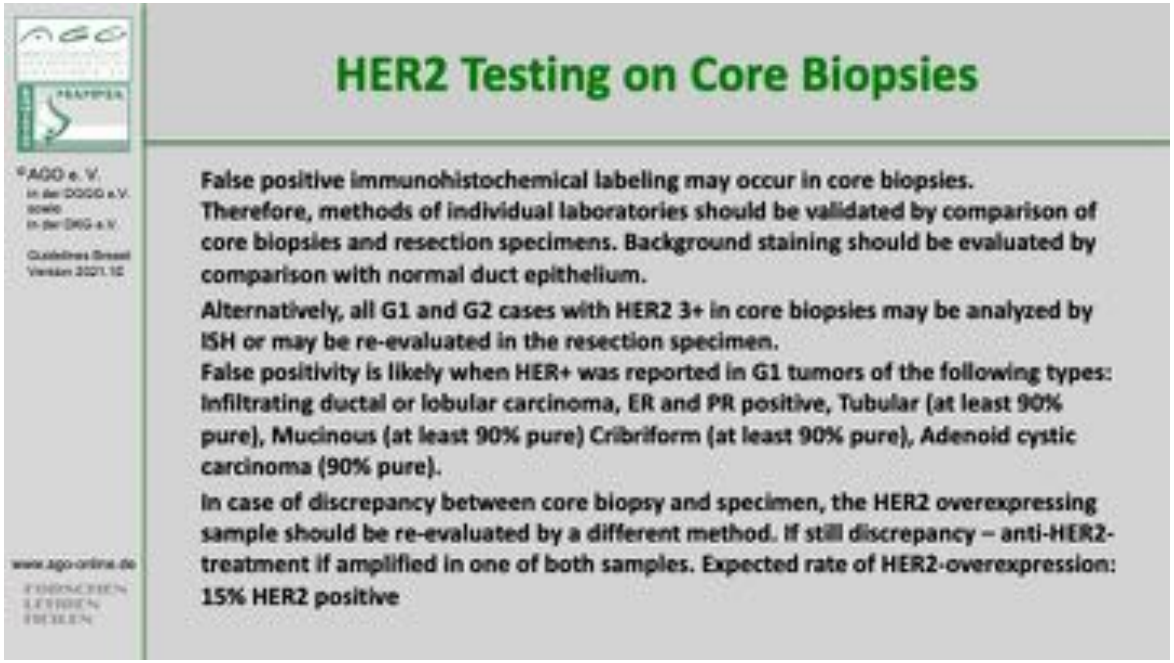

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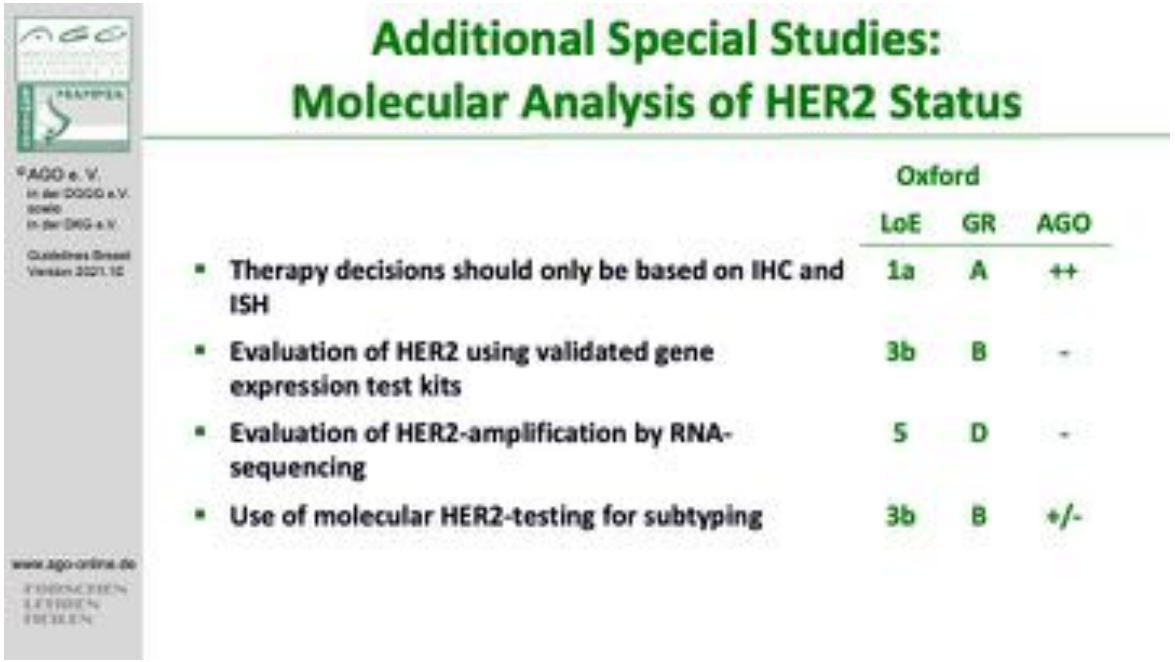

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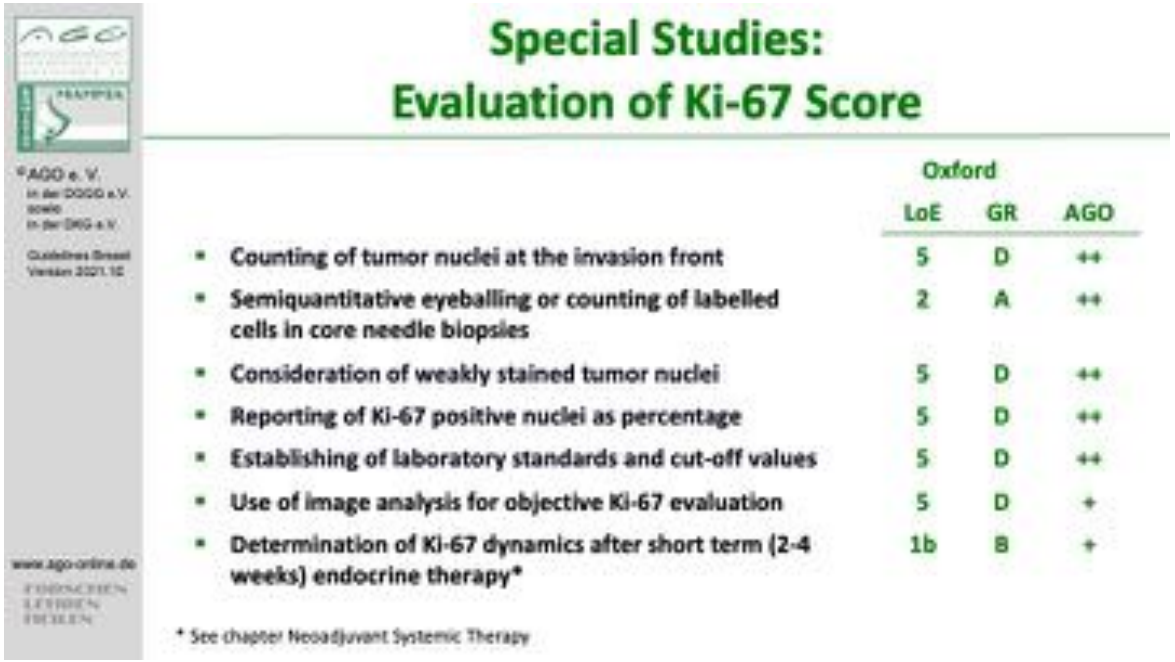

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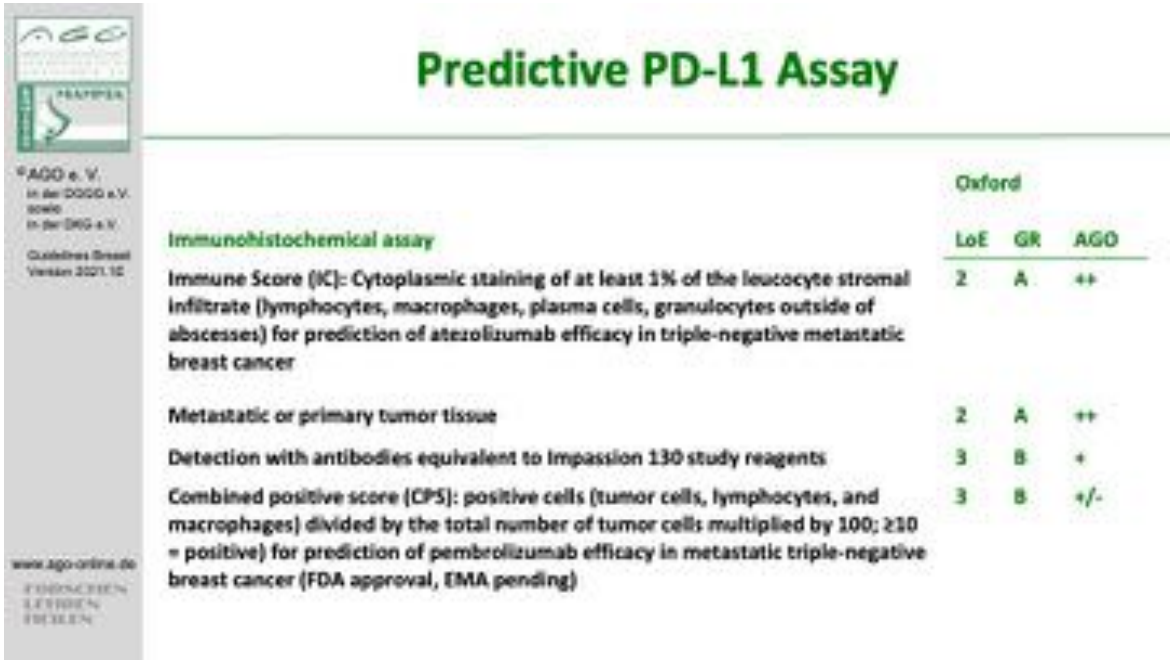

Predictive PD-L1 Assay

Immunohistochemical assay	Oxford LoE	Oxford GR	Oxford AGO
Immune Score (IC): Cytoplasmic staining of at least 1% of the leucocyte stromal infiltrate (lymphocytes, macrophages, plasma cells, granulocytes outside of abscesses) for prediction of atezolizumab efficacy in triple-negative metastatic breast cancer	2	A	++
Metastatic or primary tumor tissue	2	A	++
Detection with antibodies equivalent to Impassion 130 study reagents	3	B	+
Combined positive score (CPS): positive cells (tumor cells, lymphocytes, and macrophages) divided by the total number of tumor cells multiplied by 100; ≥10 = positive) for prediction of pembrolizumab efficacy in metastatic triple-negative breast cancer (FDA approval, EMA pending)	3	B	+/-

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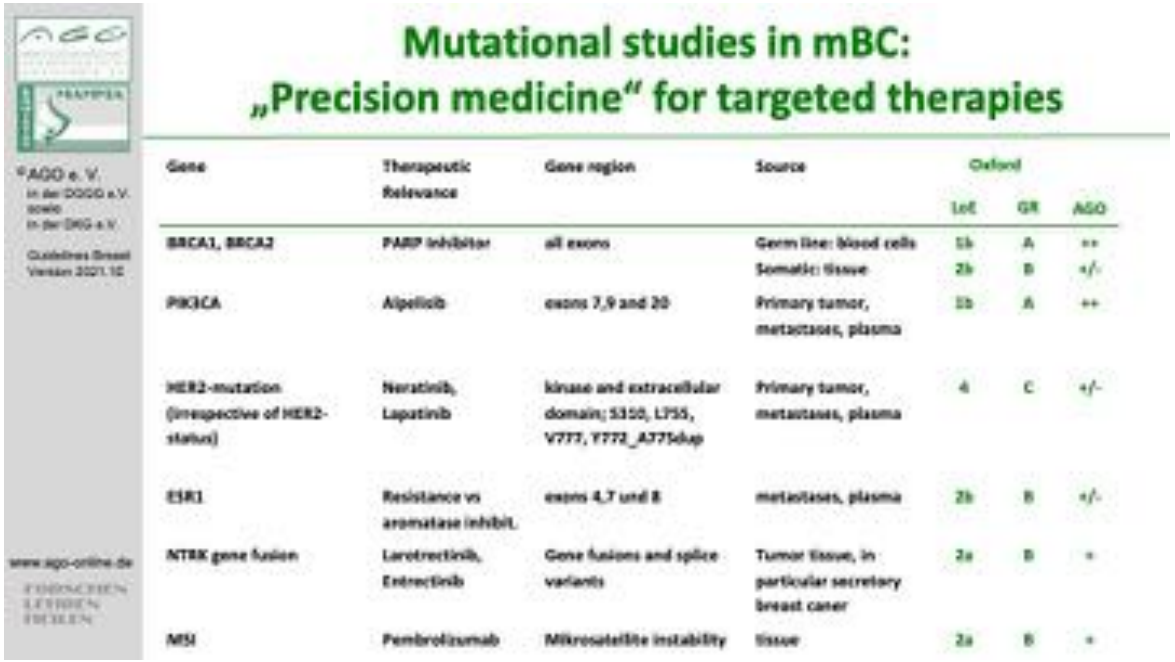

Gene	Therapeutic Relevance	Gene region	Source	Oxford LoE	Oxford GR	AGO
BRCA1, BRCA2	PARP inhibitor	all exons	Germ line: blood cells	1b	A	++
			Somatic: tissue	2b	B	+/-
PIK3CA	Alpelisib	exons 7,9 and 20	Primary tumor, metastases, plasma	1b	A	++
HER2-mutation (irrespective of HER2-status)	Neratinib, Lapatinib	kinase and extracellular domain; S310, L755, V777, Y772_A775dup	Primary tumor, metastases, plasma	4	C	+/-
ESR1	Resistance vs aromatase inhibit.	exons 4,7 und 8	metastases, plasma	2b	B	+/-
NTRK gene fusion	Larotrectinib, Entrectinib	Gene fusions and splice variants	Tumor tissue, in particular secretory breast caner	2a	B	+
MSI	Pembrolizumab	Mikrosatellite instability	tissue	2a	B	+

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MSI

FDA Zulassung entitätsübergreifend (23.5.17): Full prescribing information for pembrolizumab is available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125514s014lbl.pdf

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