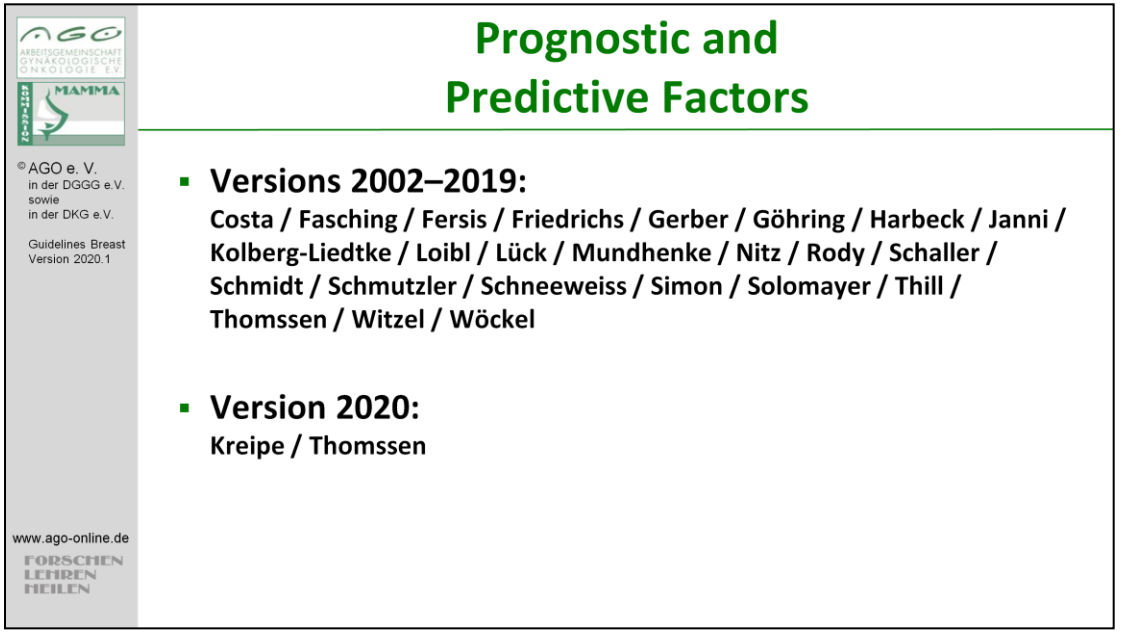
Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Guidelines Breast
Version 2020.1

FORSCHEN
LEHREN
HEILEN

Prognostic and Predictive Factors



Data bases screened

Pubmed 2008 - 2019, ASCO 2003 – 2019, SABCS 2003 – 2019, Cochrane data base (n.d.)

Guidelines screened

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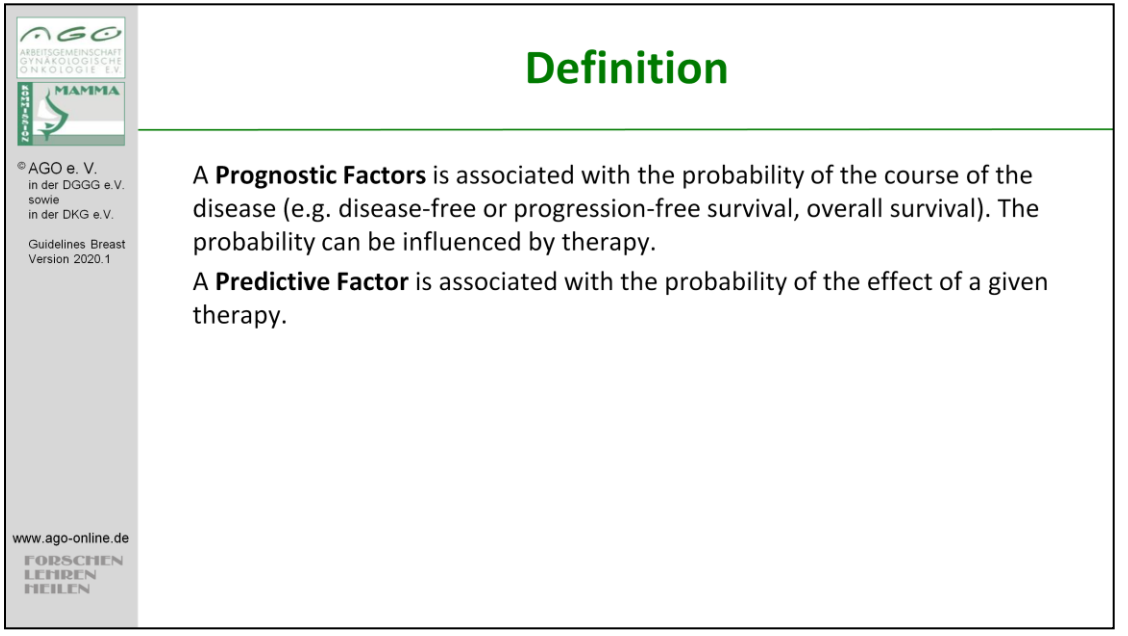

Definition of Prognosis and Prediction

Hayes DF, Bast RC, Desch CE et al.:Tumor marker utility grading system: a framework to evaluate clinical utility of tumor markers. J Natl Cancer Inst. 1996 Oct 16;88(20):1456-66.

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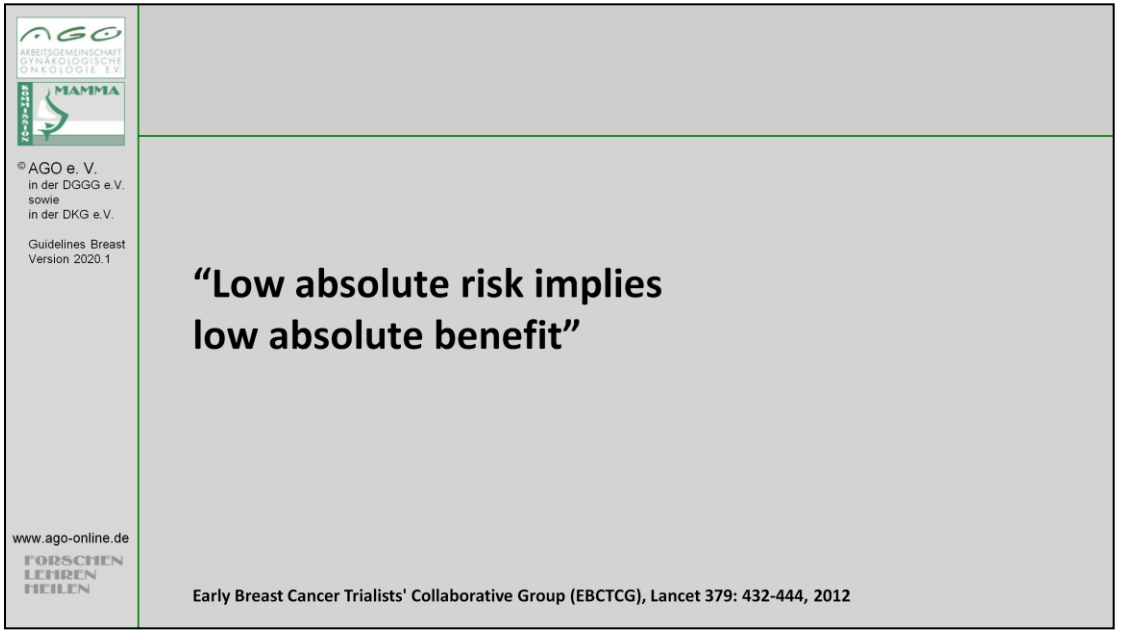

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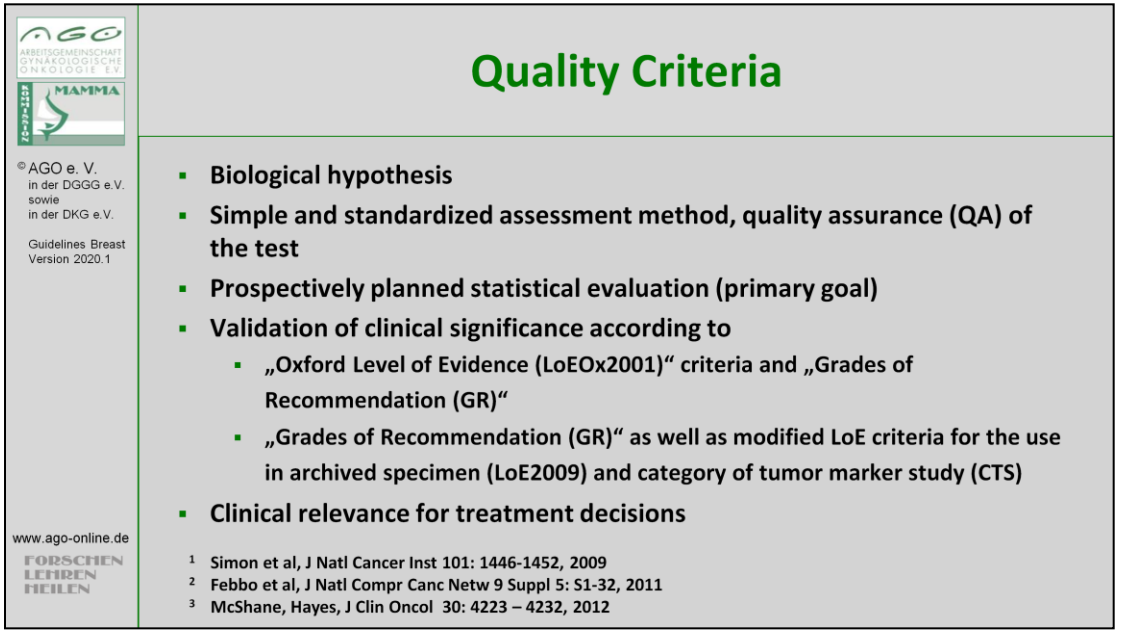

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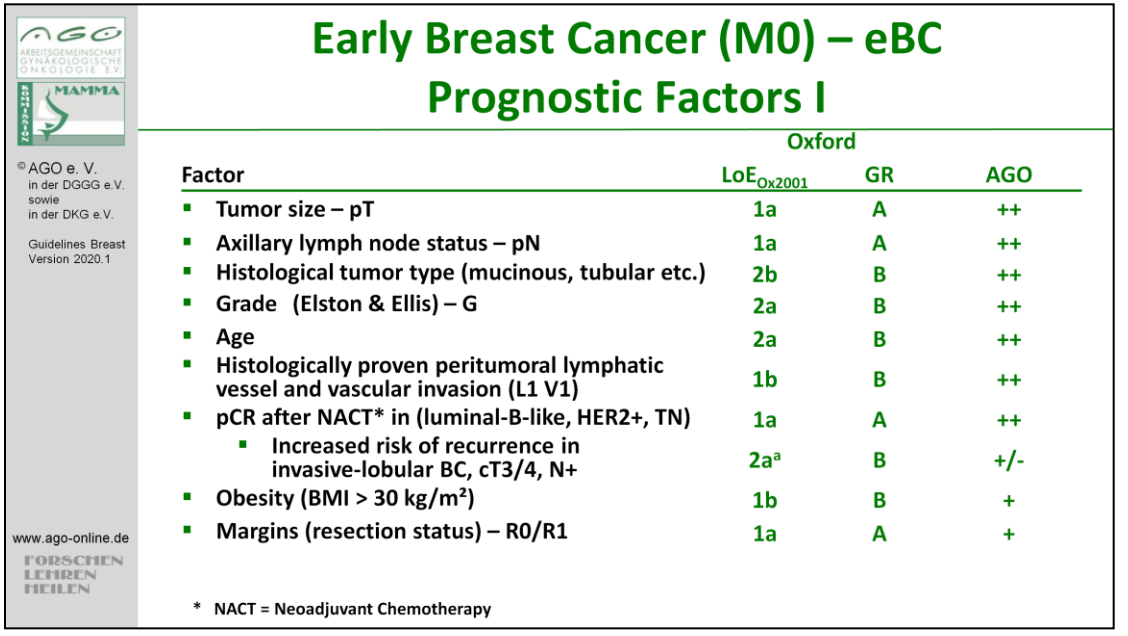

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Tumor size LoE 1a A AGO++

1. Coates AS, Winer EP, Goldhirsch A, et al. Tailoring therapies--improving the management of early breast cancer: St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2015. Ann Oncol. 2015 Aug;26(8):1533-46.

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Lymphknotenstatus LoE 1a A AGO + +

1. Coates AS, Winer EP, Goldhirsch A, et al. Tailoring therapies--improving the management of early breast cancer: St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2015. Ann Oncol. 2015 Aug;26(8):1533-46.
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Histological type (mucinous, tubular etc.) LoE 2b B AGO ++

1. Dieci MV, Orvieto E, Dominici M. Rare breast cancer subtypes: histological, molecular, and clinical peculiarities. Oncologist. 2014 Aug;19(8):805-13.
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Grading (Elston & Ellis) LoE 2a B AGO ++

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Age LoE 2a B AGO ++

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Histologically proven lymph and/or blood vessel invasion LoE 1b B AGO ++

1. Ryu YJ, Kang SJ, Cho JS et al. Lymphovascular invasion can be better than pathologic complete response to predict prognosis in breast cancer treated with neoadjuvant chemotherapy. Medicine (Baltimore). 2018 Jul;97(30):e11647

pCR after NACT* in Luminal B-like, HER2 and TN Breast Cancer ; LoE 1aA AGO ++

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4. Increased risk of recurrence in invasive-lobular BC, cT3/4, N+ LoE 2a B AGO +/-

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Obesity (BMI > 30 kg/m²) LoE 1b B AGO +

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Resection status (R0 / R1) LoE 1a A AGO +

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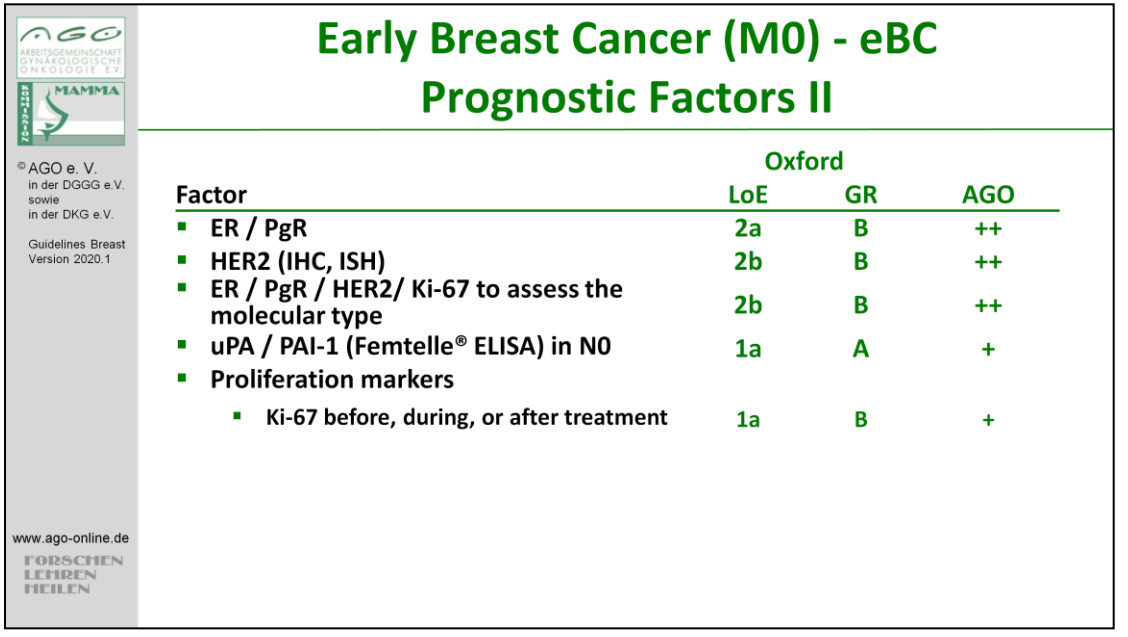

Early Breast Cancer (M0) - eBC
Prognostic Factors II

Factor	Oxford LoE	Oxford GR	AGO
▪ ER / PgR	2a	B	++
▪ HER2 (IHC, ISH)	2b	B	++
▪ ER / PgR / HER2/ Ki-67 to assess the molecular type	2b	B	++
▪ uPA / PAI-1 (Femtelle® ELISA) in N0	1a	A	+
▪ Proliferation markers			
▪ Ki-67 before, during, or after treatment	1a	B	+

ER/PR

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uPA/PAI-1

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Ki-67

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Post-treatment Ki-67

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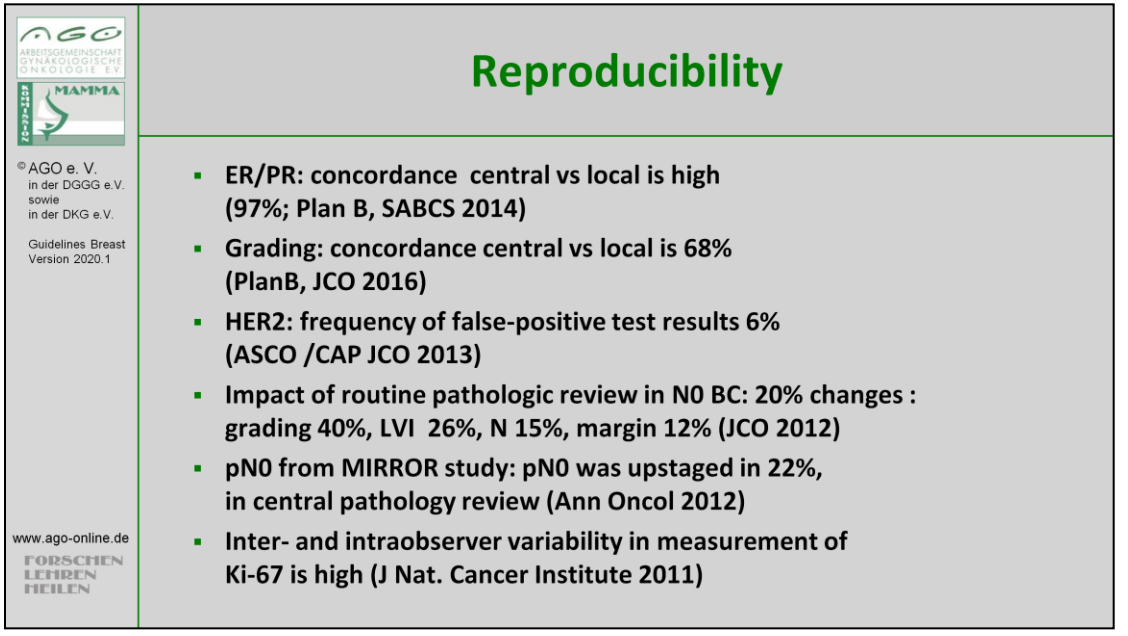

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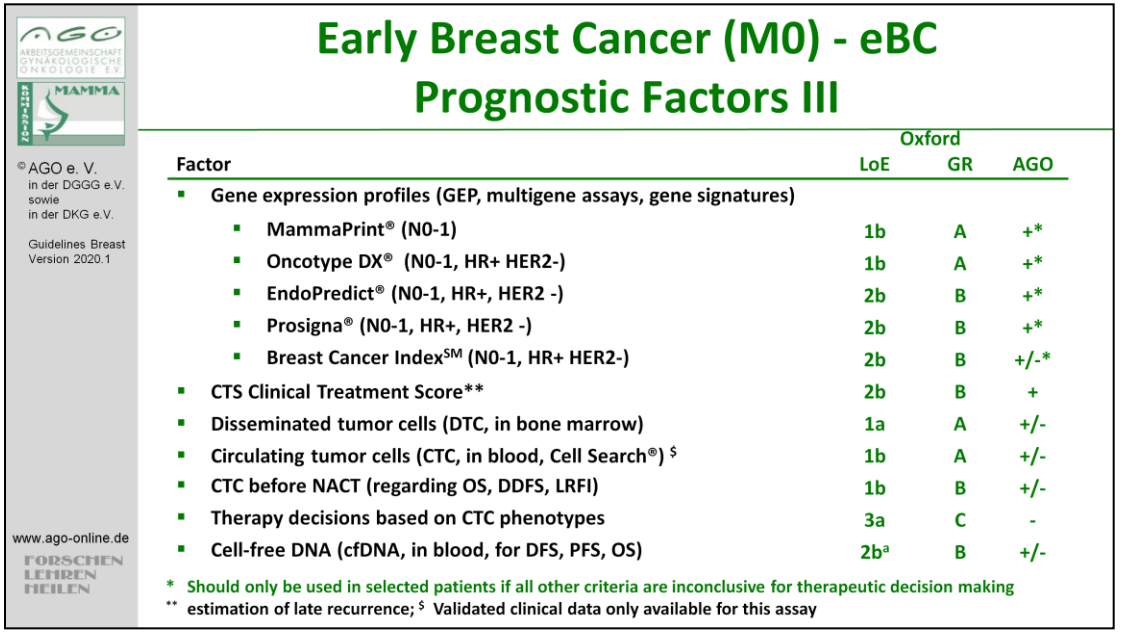

Early Breast Cancer (M0) - eBC
Prognostic Factors III

Factor	Oxford LoE	Oxford GR	Oxford AGO
▪ Gene expression profiles (GEP, multigene assays, gene signatures)			
▪ MammaPrint® (N0-1)	1b	A	+*
▪ Oncotype DX® (N0-1, HR+ HER2-)	1b	A	+*
▪ EndoPredict® (N0-1, HR+, HER2 -)	2b	B	+*
▪ Prosigna® (N0-1, HR+, HER2 -)	2b	B	+*
▪ Breast Cancer Index^{SM} (N0-1, HR+ HER2-)	2b	B	+/-*
▪ CTS Clinical Treatment Score**	2b	B	+
▪ Disseminated tumor cells (DTC, in bone marrow)	1a	A	+/-
▪ Circulating tumor cells (CTC, in blood, Cell Search®) $	1b	A	+/-
▪ CTC before NACT (regarding OS, DDFS, LRFI)	1b	B	+/-
▪ Therapy decisions based on CTC phenotypes	3a	C	-
▪ Cell-free DNA (cfDNA, in blood, for DFS, PFS, OS)	2b[a]	B	+/-

* Should only be used in selected patients if all other criteria are inconclusive for therapeutic decision making
** estimation of late recurrence; $ Validated clinical data only available for this assay

Genexpressionsprofile (GEP; Multigene Assays, Gensignaturen)

(*Should only be used in selected patients if all other criteria are inconclusive for therapeutic decision making)

MammaPrint® (N0-1) LoE 1b A AGO+*

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Oncotype DX® (N0-1, HR+, HER2-) LoE 1b A AGO +*

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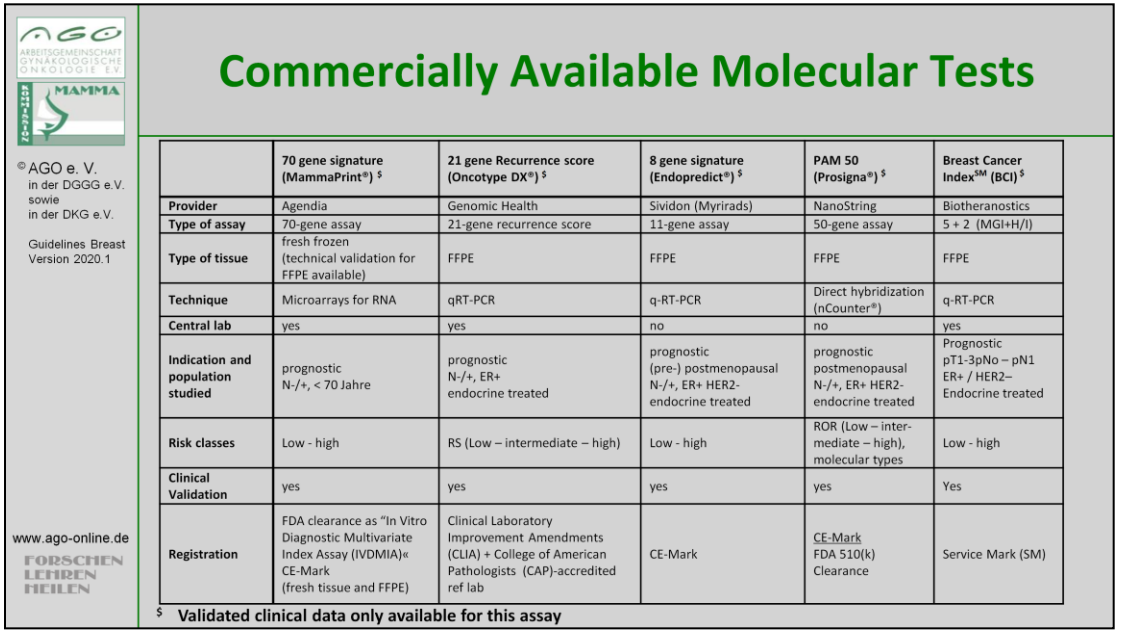

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Breast Cancer IndexSM (N0-1, HR+ HER2-) LoE 2b B AGO +/-*

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Multiple assays

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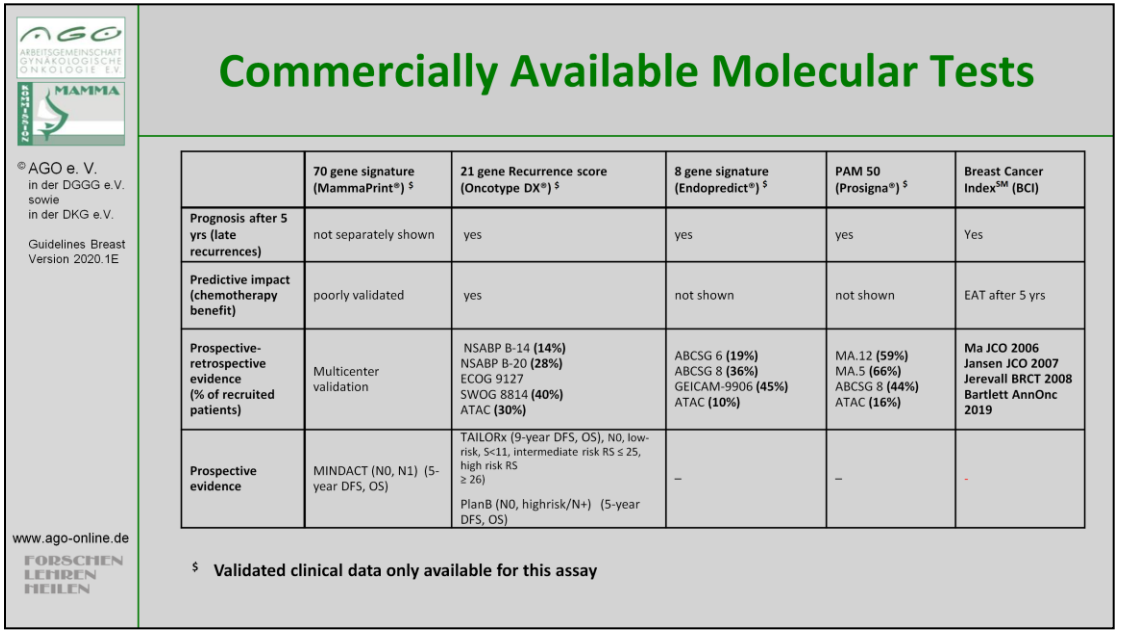

	70 gene signature (MammaPrint®) $	21 gene Recurrence score (Oncotype DX®) $	8 gene signature (Endopredict®) $	PAM 50 (Prosigna®) $	Breast Cancer Index^{SM} (BCI)
Prognosis after 5 yrs (late recurrences)	not separately shown	yes	yes	yes	Yes
Predictive impact (chemotherapy benefit)	poorly validated	yes	not shown	not shown	EAT after 5 yrs
Prospective-retrospective evidence (% of recruited patients)	Multicenter validation	NSABP B-14 **(14%)** NSABP B-20 **(28%)** ECOG 9127 SWOG 8814 **(40%)** ATAC **(30%)**	ABCSG 6 **(19%)** ABCSG 8 **(36%)** GEICAM-9906 **(45%)** ATAC **(10%)**	MA.12 **(59%)** MA.5 **(66%)** ABCSG 8 **(44%)** ATAC **(16%)**	**Ma JCO 2006** **Jansen JCO 2007** **Jerevall BRCT 2008** **Bartlett AnnOnc 2019**
Prospective evidence	MINDACT (N0, N1) (5-year DFS, OS)	TAILORx (9-year DFS, OS), N0, low-risk, S<11, intermediate risk RS ≤ 25, high risk RS ≥ 26) PlanB (N0, highrisk/N+) (5-year DFS, OS)	–	–	-

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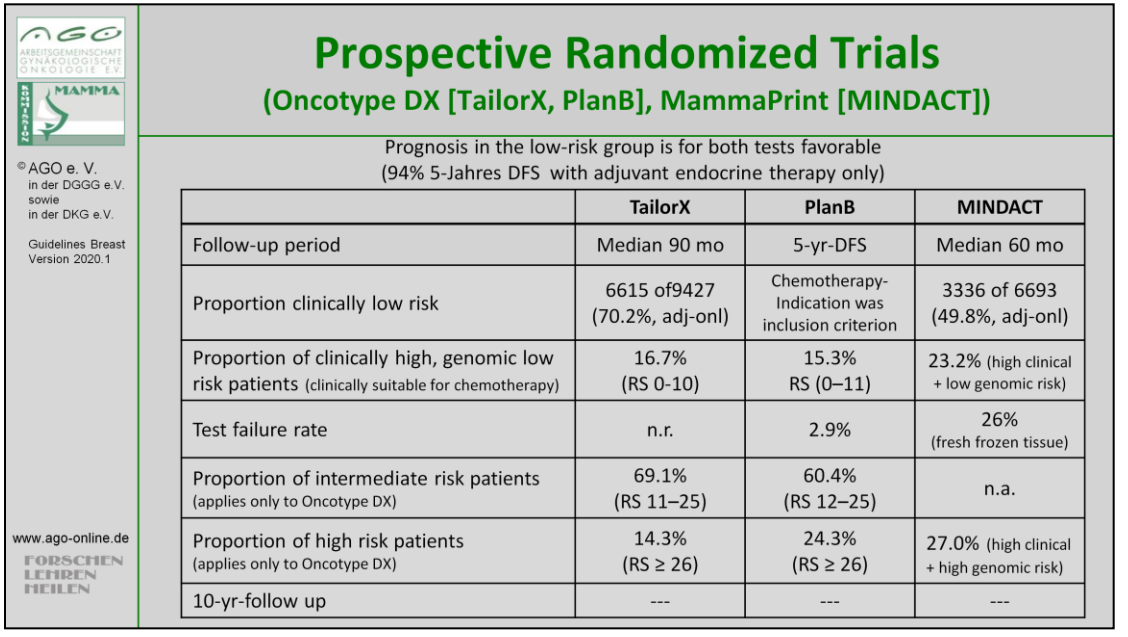

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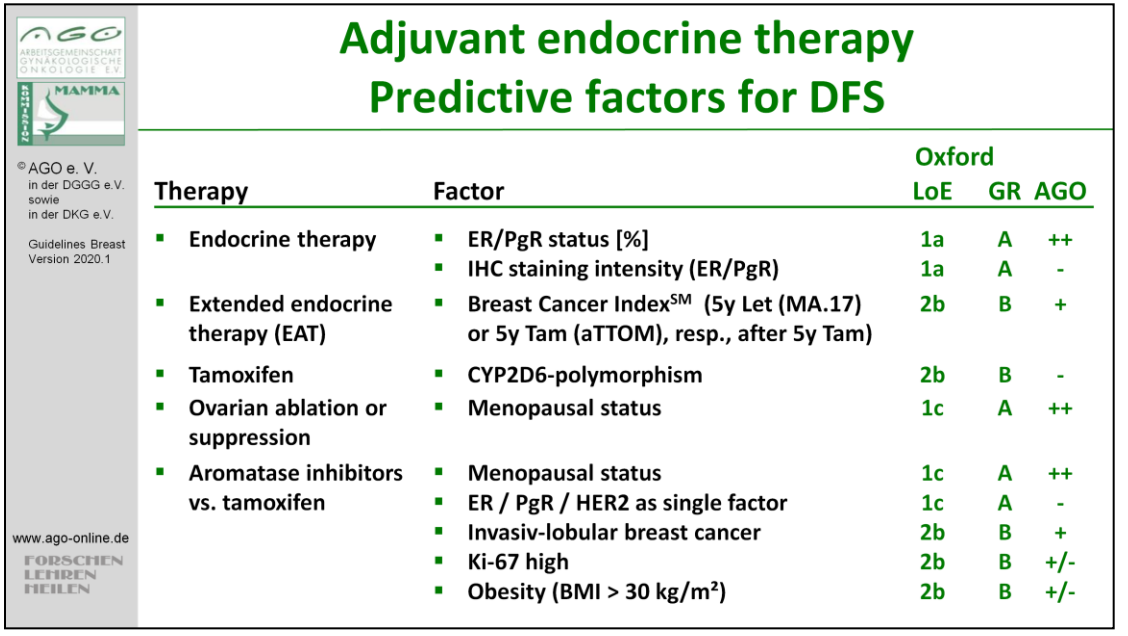

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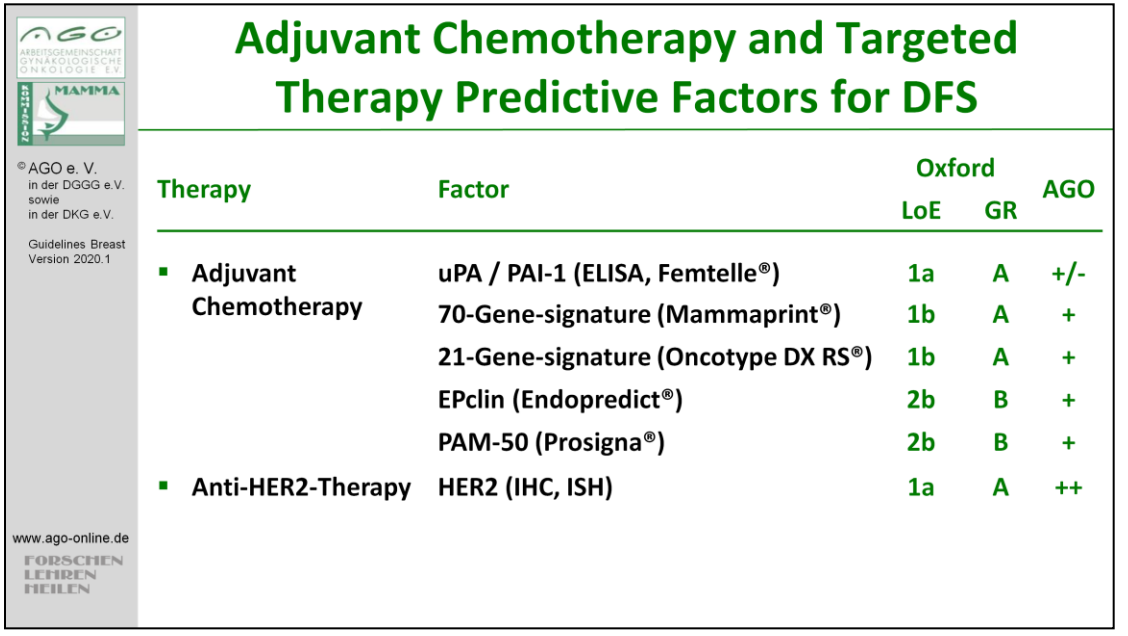

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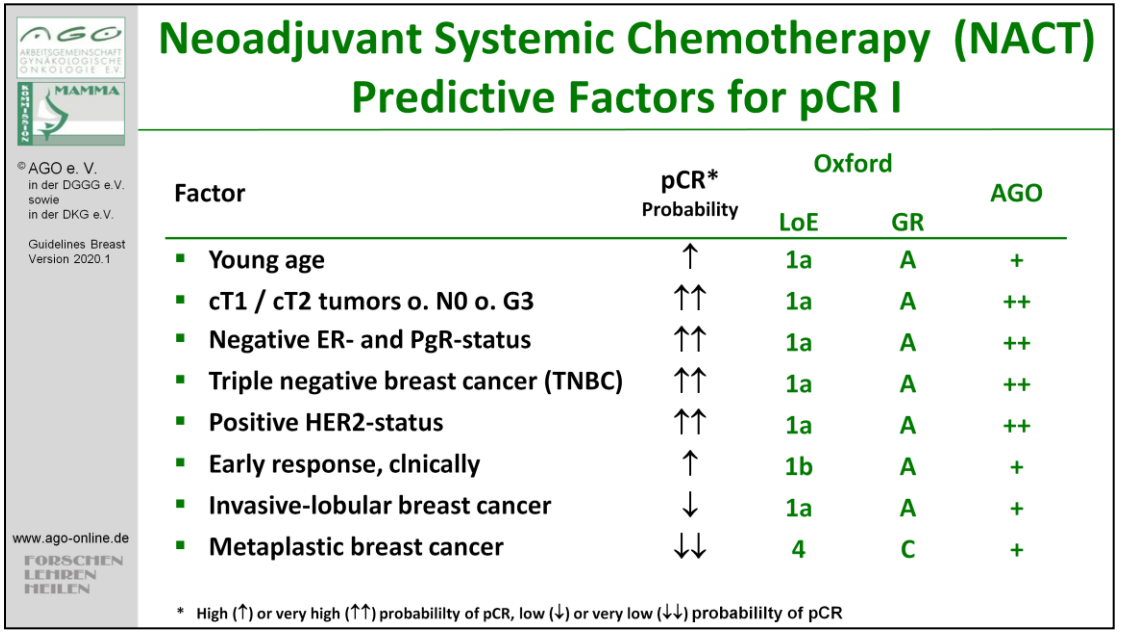

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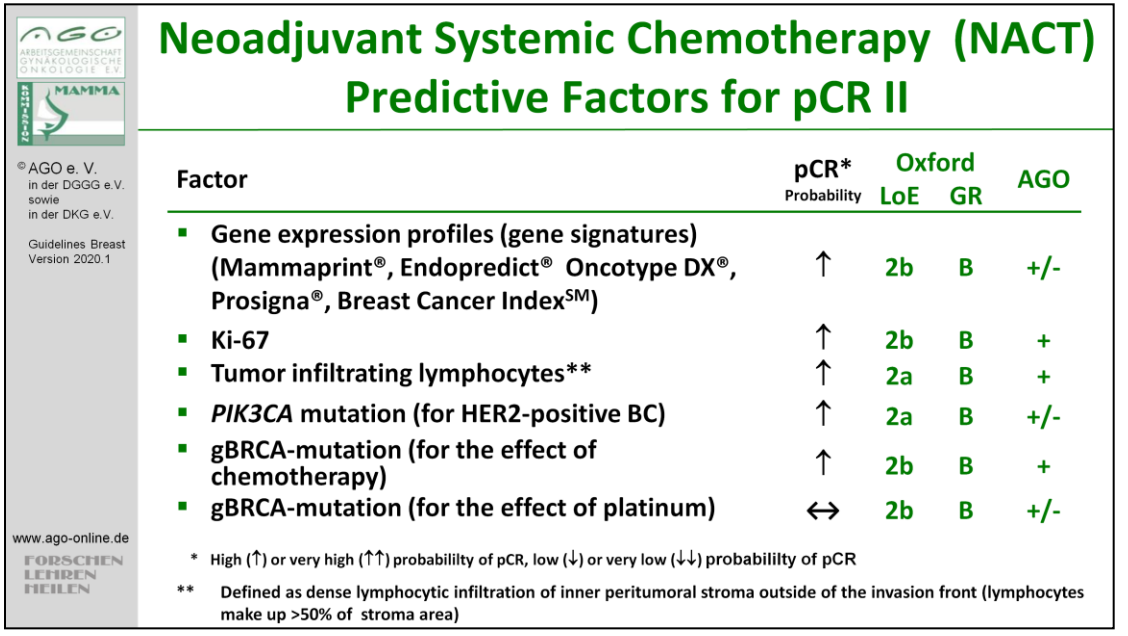

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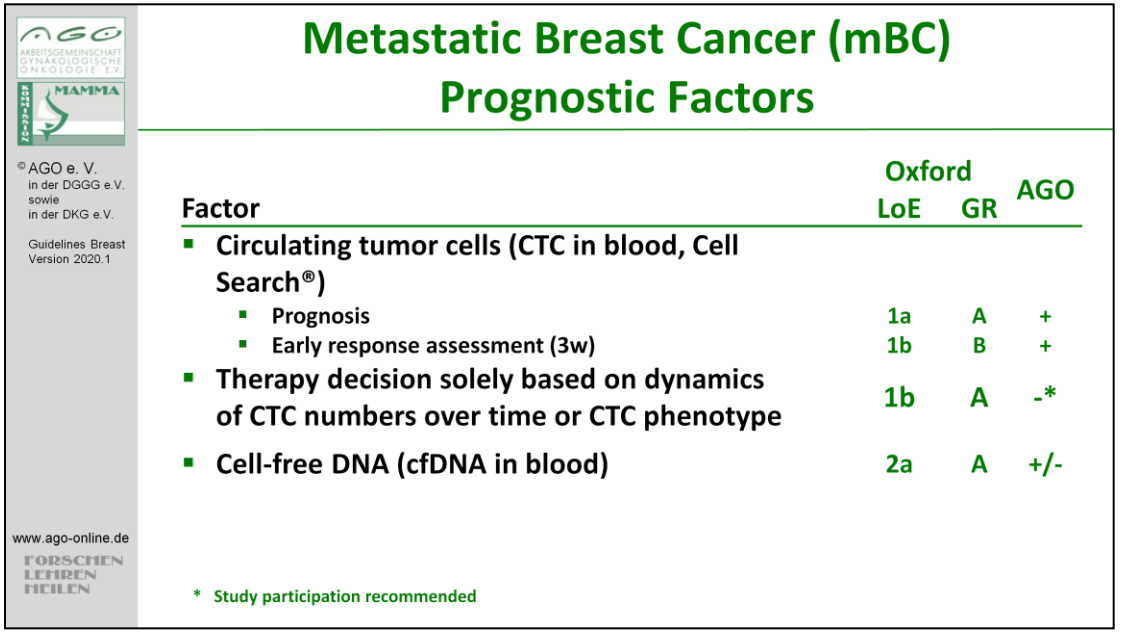

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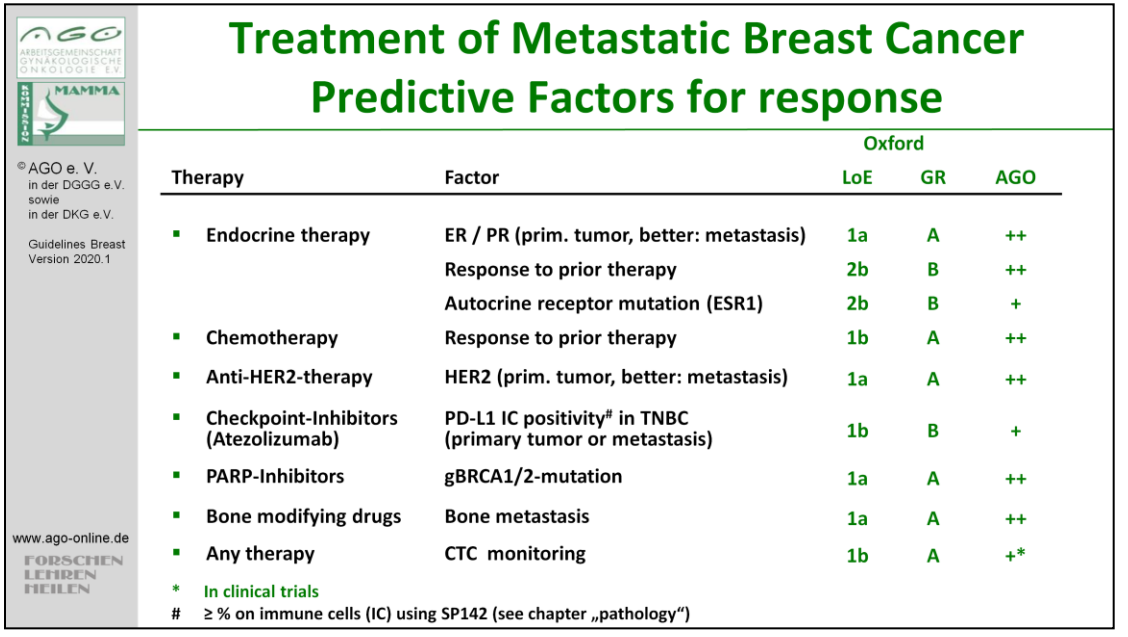

Treatment of Metastatic Breast Cancer
Predictive Factors for response

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Therapy	Factor	Oxford LoE	Oxford GR	AGO
▪ Endocrine therapy	ER / PR (prim. tumor, better: metastasis)	1a	A	++
	Response to prior therapy	2b	B	++
	Autocrine receptor mutation (ESR1)	2b	B	+
▪ Chemotherapy	Response to prior therapy	1b	A	++
▪ Anti-HER2-therapy	HER2 (prim. tumor, better: metastasis)	1a	A	++
▪ Checkpoint-Inhibitors (Atezolizumab)	PD-L1 IC positivity# in TNBC (primary tumor or metastasis)	1b	B	+
▪ PARP-Inhibitors	gBRCA1/2-mutation	1a	A	++
▪ Bone modifying drugs	Bone metastasis	1a	A	++
▪ Any therapy	CTC monitoring	1b	A	+*

* In clinical trials
\# ≥ % on immune cells (IC) using SP142 (see chapter „pathology“)

Endocrine therapy

ER/PR (Primärtumor, besser Metastase)

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Anti-HER2-Therapy

HER2 (primary, better: metastasis

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Checkpoint-Inhibitoren

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PARP-Inhibitoren

gBRCA-mutations

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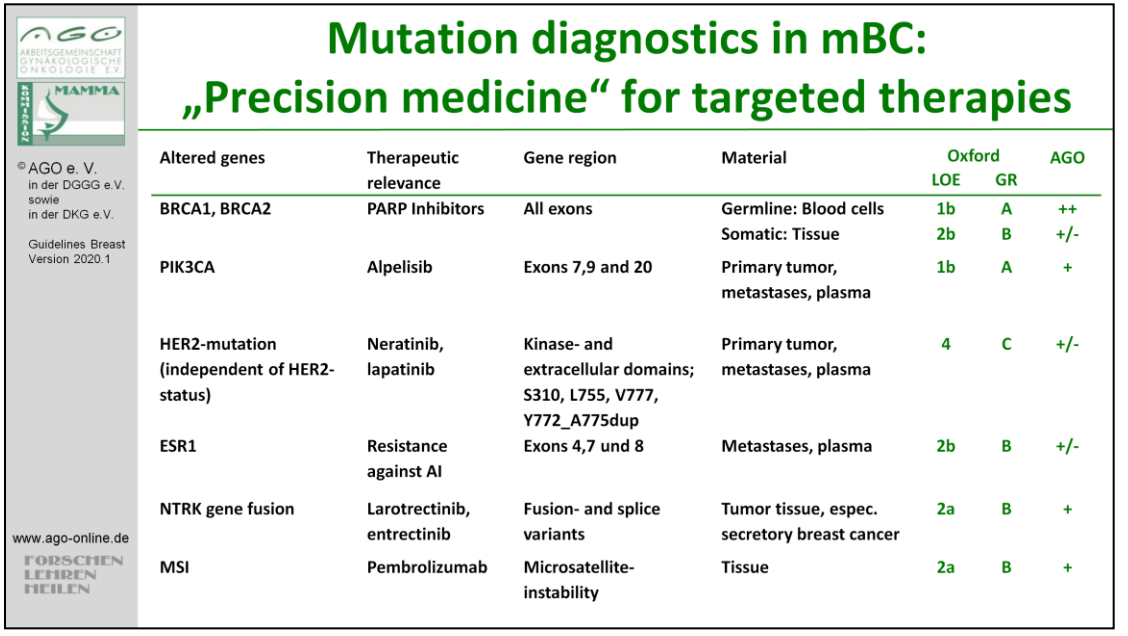

Altered genes	Therapeutic relevance	Gene region	Material	Oxford LOE	Oxford GR	AGO
BRCA1, BRCA2	PARP Inhibitors	All exons	Germline: Blood cells	1b	A	++
			Somatic: Tissue	2b	B	+/-
PIK3CA	Alpelisib	Exons 7,9 and 20	Primary tumor, metastases, plasma	1b	A	+
HER2-mutation (independent of HER2-status)	Neratinib, lapatinib	Kinase- and extracellular domains; S310, L755, V777, Y772_A775dup	Primary tumor, metastases, plasma	4	C	+/-
ESR1	Resistance against AI	Exons 4,7 und 8	Metastases, plasma	2b	B	+/-
NTRK gene fusion	Larotrectinib, entrectinib	Fusion- and splice variants	Tumor tissue, espec. secretory breast cancer	2a	B	+
MSI	Pembrolizumab	Microsatellite-instability	Tissue	2a	B	+

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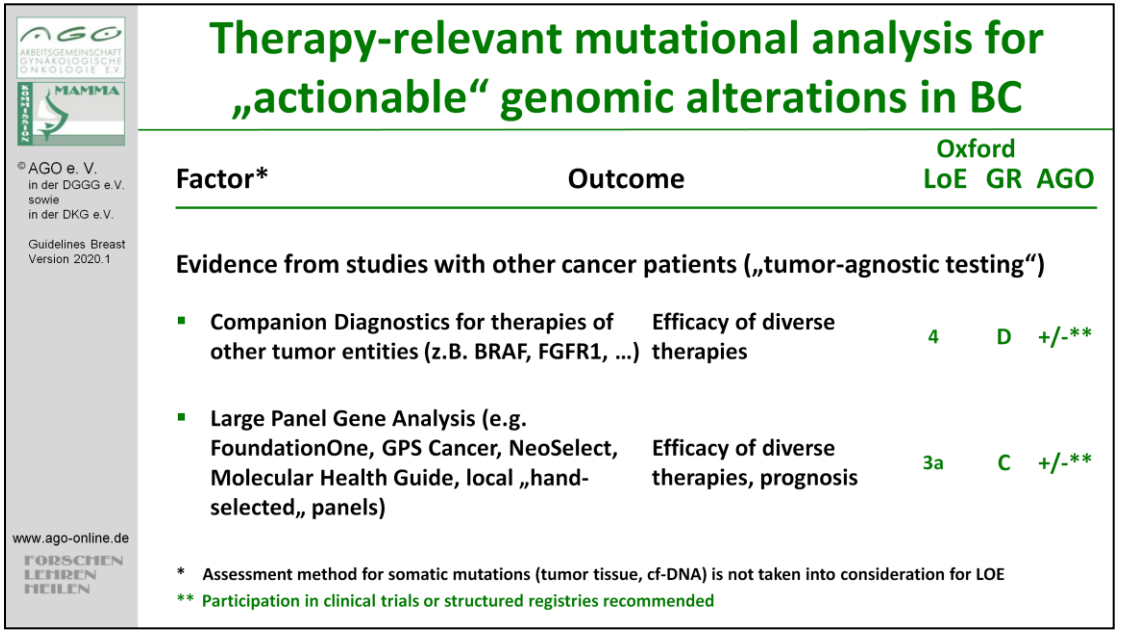

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