Screened data bases

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Screened guidelines

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Supportive Therapie und Nebenwirkungsmanagement

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1. S3-Leitlinie Supportive Therapie:
   Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3 – Februar 2020 AWMF-Registernummer: 032/054OL Zugriff 25.12.2021 https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Supportivtherapie/LL_Supportiv_Langversion_1.3.pdf

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Toxizitätsbeurteilung

- **Akute Toxizität (NCI-CTCAE)**
- **Langzeittoxizität (ICPC, ICD-GM)**

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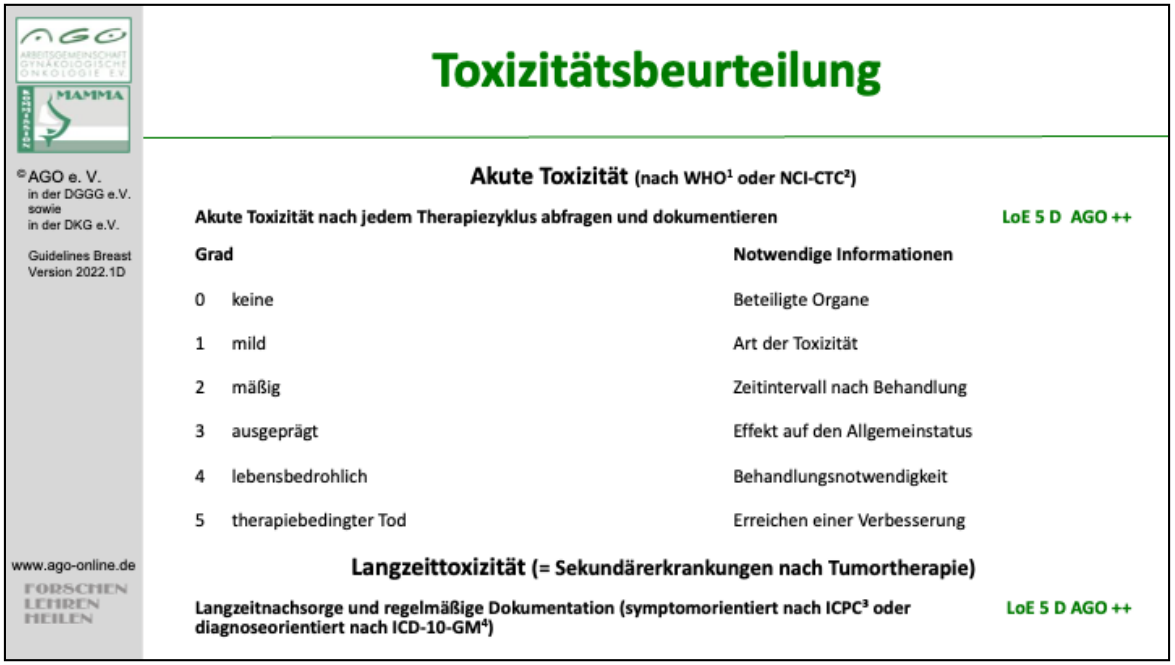

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Langzeittoxizität

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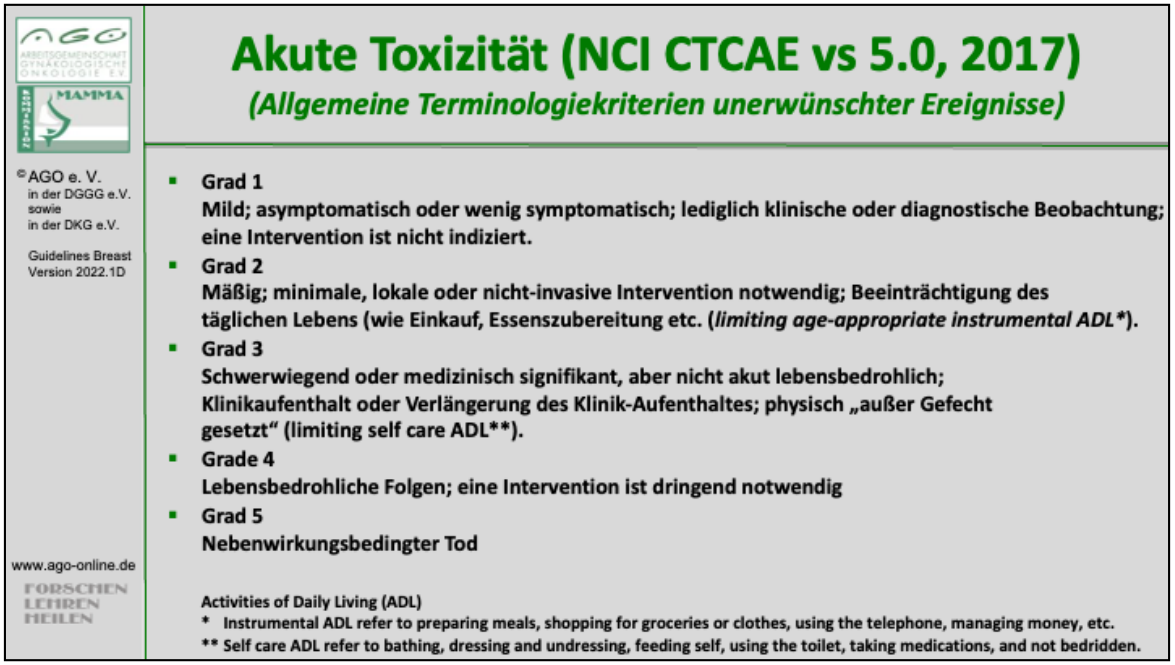

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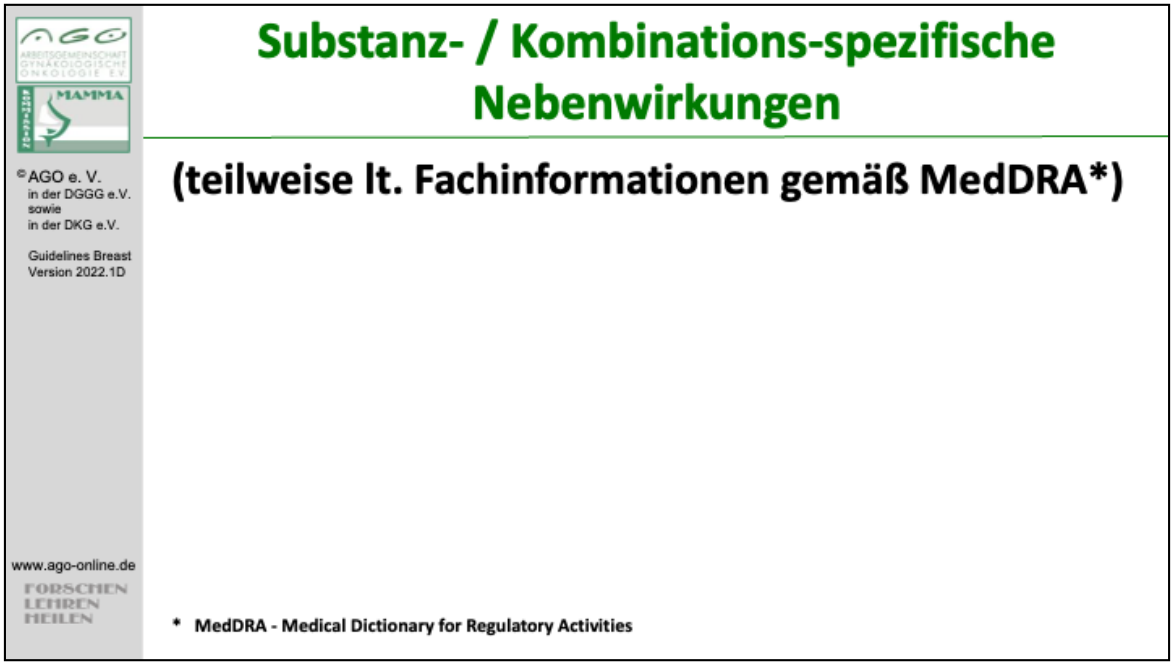
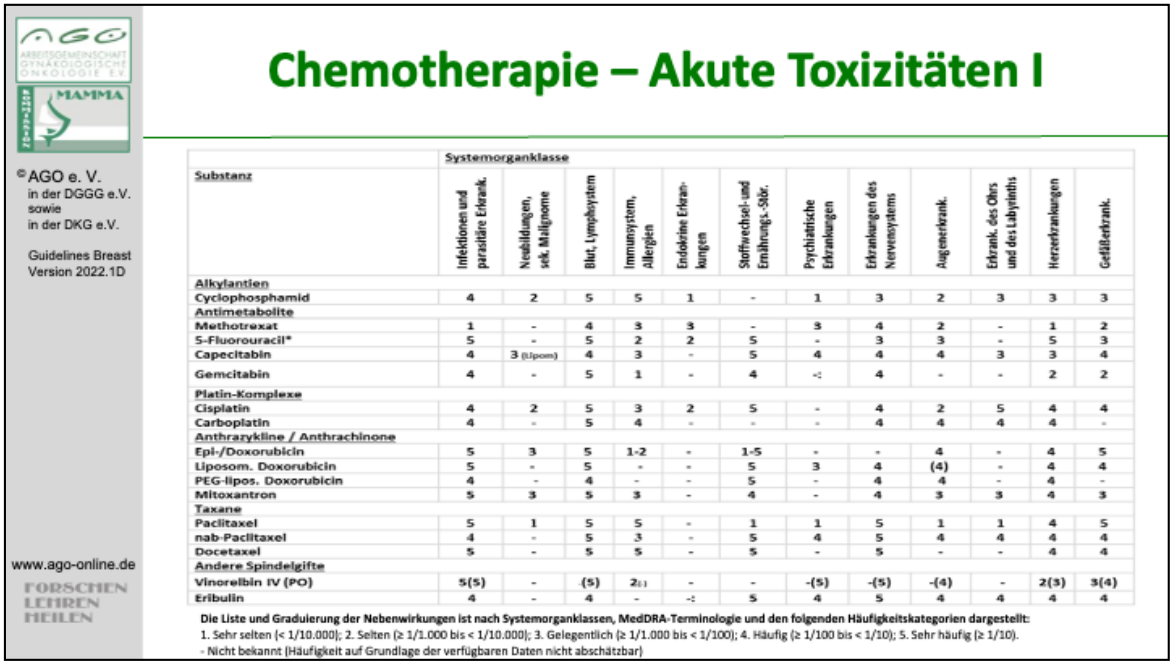


*MedDRA - Medical Dictionary for Regulatory Activities

https://www.meddra.org/



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Substanz	Systemorganklasse											
	Infektionen und parasitäre Erkrank.	Neubildungen, inkl. Malignome	Blut, Lymphsystem	Immunsystem, Allergien	Endokrine Erkrankungen	Stoffwechsel- und Ernährungs.-Stör.	Psychiatrische Erkrankungen	Erkrankungen des Nervensystems	Augenerkrank.	Erkrank. des Ohrs und des Labyrinths	Herzerkrankungen	Gefäßerkrank.
Alkylantien												
Cyclophosphamid	4	2	5	5	1	-	1	3	2	3	3	3
Antimetabolite												
Methotrexat	1	-	4	3	3	-	3	4	2	-	1	2
5-Fluorouracil*	5	-	5	2	2	5	-	3	3	-	5	3
Capecitabin	4	3 (Lipom)	4	3	-	5	4	4	4	3	3	4
Gemcitabin	4	-	5	1	-	4	-:	4	-	-	2	2
Platin-Komplexe												
Cisplatin	4	2	5	3	2	5	-	4	2	5	4	4
Carboplatin	4	-	5	4	-	-	-	4	4	4	4	-
Anthrazykline / Anthrachinone												
Epi-/Doxorubicin	5	3	5	1-2	-	1-5	-	-	4	-	4	5
Liposom. Doxorubicin	5	-	5	-	-	5	3	4	(4)	-	4	4
PEG-lipos. Doxorubicin	4	-	4	-	-	5	-	4	4	-	4	-
Mitoxantron	5	3	5	3	-	4	-	4	3	3	4	3
Taxane												
Paclitaxel	5	1	5	5	-	1	1	5	1	1	4	5
nab-Paclitaxel	4	-	5	3	-	5	4	5	4	4	4	4
Docetaxel	5	-	5	5	-	5	-	5	-	-	4	4
Andere Spindelgifte												
Vinorelbin IV (PO)	5(5)	-	(5)	2(1)	-	-	-(5)	-(5)	-(4)	-	2(3)	3(4)
Eribulin	4	-	4	-	-:	5	4	5	4	4	4	4

Die Liste und Graduierung der Nebenwirkungen ist nach Systemorganklassen, MedDRA-Terminologie und den folgenden Häufigkeitskategorien dargestellt:
1. Sehr selten (< 1/10.000); 2. Selten (≥ 1/1.000 bis < 1/10.000); 3. Gelegentlich (≥ 1/1.000 bis < 1/100); 4. Häufig (≥ 1/100 bis < 1/10); 5. Sehr häufig (≥ 1/10).
- Nicht bekannt (Häufigkeit auf Grundlage der verfügbaren Daten nicht abschätzbar)

Nebenwirkungskategorien - MedDRA (Medical Dictionary for Regulatory Activities)

1. MedDRA: https://www.meddra.org/ bzw. https://www.meddra.org/sites/default/files/guidance/file/intguide_20_1_english_0.pdf

Quellen für die Fachinformationen (Download 19.01.2018)

1. Cyclophosphamid: http://www.baxter.de/de_DE/assets/downloads/fachinformation/endoxan.pdf
2. Methotrexat: https://www.gelbe-liste.de/produkte/MTX-HEXAL-10-mg-Tabletten_117469/fachinformation
3. 5-Fluorouracil: https://www.gelbe-liste.de/produkte/Fluorouracil-HEXAL-50-mg-ml-Injektionsloesung-100-ml_546519/fachinformation
4. Capecitabin: https://www.zentiva.de/Produkte/Capecitabin-Zentiva/Downloads?id=a63946ee-51ce-46ac-8184-a468b705ed9b
5. Gemcitabin: http://www.success-studie.de/b/downloads/Fachinfo/GemzarFI07Jan.pdf
6. Cisplatin: https://www.gelbe-liste.de/produkte/Cisplatin-Teva-1-mg-ml-Konzentrat-zur-Herstellung-einer-Infusionsloesung-100-ml_543960/fachinformation
7. Carboplatin: http://www.teva.de/index.php?eID=dumpFile&t=f&f=37532&g=-1&r=11068%2C11068&token=eebfb22e78f1cc8d9935d59c087e80630146f49e

8. Epirubicin:
9. Doxorubicin:
10. Liposomales Doxorubicin: https://www.gelbe-liste.de/produkte/Myocet-50-mg-Pulver-Dispersion-u-Loesungsmittel-fuer-ein-Konzentrat-zur-Herstellung-einer-Infusionsdispersion_359323/fachinformation
11. PEG-lipo. Doxorubicin: https://www.gelbe-liste.de/produkte/Caelyx-2-mg-ml-Konzentrat-zur-Herstellung-einer-Infusionsloesung-10-ml_121890/fachinformation
12. Mitoxantron: https://www.gelbe-liste.de/produkte/Mitoxantron-Teva-2-mg-ml-Injektionsloesung-15ml_543783/fachinformation
13. Paclitaxel: https://medikamio.com/de-de/medikamente/paclitaxel-ratiopharm/pil
14. Nab-Paclitaxel: https://www.gelbe-liste.de/produkte/Abraxane-5-mg-ml-Pulver-zur-Herstellung-einer-Infusionssuspension_514889/fachinformation
15. Docetaxel: https://mein.sanofi.de/produkte/Taxotere/Downloads?id=89447754-dfb2-450b-b35a-36950de8a74d
16. Vinorelbin: http://www.detect-studien.de/dokumente/d3/fachinfo/Navelbine.pdf
17. Eribulin: http://www.detect-studien.de/dokumente/d4/fachinfo/Fachinfo_Eribulin_Halaven.pdf

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3. Jim HS et al: Meta-analysis of cognitive functioning in breast cancer survivors previously treated with standard-dose chemotherapy. J Clin Oncol. 2012 Oct 10;30(29):3578-87
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6. Fox P, Darley A, Furlong E, et al: The assessment and management of chemotherapy-related toxicities in patients with breast cancer, colorectal cancer, and Hodgkin's and non-Hodgkin's lymphomas: A scoping review. Eur J Oncol Nurs. 2017 Feb;26:63-82. doi: 10.1016/j.ejon.2016.12.008. Epub 2016 Dec 22.

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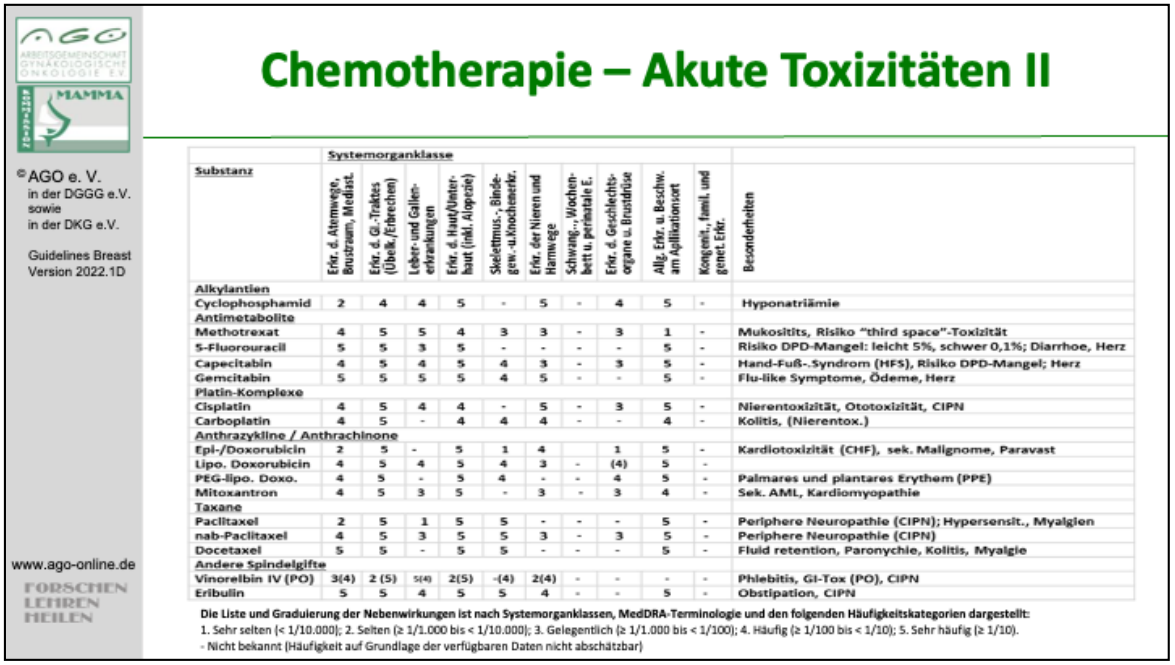

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Substanz	Systemorganklasse: Erkr. d. Atemwege, Brustraum, Mediast.	Erkr. d. GI.-Traktes (Übelk./Erbrechen)	Leber- und Gallenerkrankungen	Erkr. d. Haut/Unterhaut (inkl. Alopezie)	Skelettmus.-, Bindegew.-u.Knochenerkr.	Erkr. der Nieren und Harnwege	Schwang.-, Wochenbett u. perinatale E.	Erkr. d. Geschlechtsorgane u. Brustdrüse	Allg. Erkr. u. Beschw. am Applikationsort	Kongenit., famil. und genet. Erkr.	Besonderheiten
Alkylantien											
Cyclophosphamid	2	4	4	5	-	5	-	4	5	-	Hyponatriämie
Antimetabolite											
Methotrexat	4	5	5	4	3	3	-	3	1	-	Mukositits, Risiko "third space"-Toxizität
5-Fluorouracil	5	5	3	5	-	-	-	-	5	-	Risiko DPD-Mangel: leicht 5%, schwer 0,1%; Diarrhoe, Herz
Capecitabin	4	5	4	5	4	3	-	3	5	-	Hand-Fuß-.Syndrom (HFS), Risiko DPD-Mangel; Herz
Gemcitabin	5	5	5	5	4	5	-	-	5	-	Flu-like Symptome, Ödeme, Herz
Platin-Komplexe											
Cisplatin	4	5	4	4	-	5	-	3	5	-	Nierentoxizität, Ototoxizität, CIPN
Carboplatin	4	5	-	4	4	4	-	-	4	-	Kolitis, (Nierentox.)
Anthrazykline / Anthrachinone											
Epi-/Doxorubicin	2	5	-	5	1	4		1	5	-	Kardiotoxizität (CHF), sek. Malignome, Paravast
Lipo. Doxorubicin	4	5	4	5	4	3	-	(4)	5	-	
PEG-lipo. Doxo.	4	5	-	5	4	-	-	4	5	-	Palmares und plantares Erythem (PPE)
Mitoxantron	4	5	3	5	-	3	-	3	4	-	Sek. AML, Kardiomyopathie
Taxane											
Paclitaxel	2	5	1	5	5	-	-	-	5	-	Periphere Neuropathie (CIPN); Hypersensit., Myalgien
nab-Paclitaxel	4	5	3	5	5	3	-	3	5	-	Periphere Neuropathie (CIPN)
Docetaxel	5	5	-	5	5	-	-	-	5	-	Fluid retention, Paronychie, Kolitis, Myalgie
Andere Spindelgifte											
Vinorelbin IV (PO)	3(4)	2 (5)	5(4)	2(5)	-(4)	2(4)	-	-	-	-	Phlebitis, GI-Tox (PO), CIPN
Eribulin	5	5	4	5	5	4	-	-	5	-	Obstipation, CIPN

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- Nicht bekannt (Häufigkeit auf Grundlage der verfügbaren Daten nicht abschätzbar)

Abkürzungen

AML = Akute myeloische Leukämie; DPD = Dihydropyrimidin-Dehydrogenase); CHF = Kardiomyopathie; CIPN = Chemotherapie induzierte periphere Neuropathie; HFS = Hand-Fuß-Syndrom; PPE = Palmares und plantares Erythem.

Nebenwirkungskategorien - MedDRA (Medical Dictionary for Regulatory Activities)

1. MedDRA: https://www.meddra.org/ bzw. https://www.meddra.org/sites/default/files/guidance/file/intguide_20_1_english_0.pdf

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1. Cyclophosphamid: http://www.baxter.de/de_DE/assets/downloads/fachinformation/endoxan.pdf
2. Methotrexat: https://www.gelbe-liste.de/produkte/MTX-HEXAL-10-mg-Tabletten_117469/fachinformation
3. 5-Fluorouracil: https://www.gelbe-liste.de/produkte/Fluorouracil-HEXAL-50-mg-ml-Injektionsloesung-100-ml_546519/fachinformation
4. Capecitabin: https://www.zentiva.de/Produkte/Capecitabin-Zentiva/Downloads?id=a63946ee-51ce-46ac-8184-a468b705ed9b
5. Gemcitabin: http://www.success-studie.de/b/downloads/Fachinfo/GemzarFI07Jan.pdf

6. Cisplatin: https://www.gelbe-liste.de/produkte/Cisplatin-Teva-1-mg-ml-Konzentrat-zur-Herstellung-einer-Infusionsloesung-100-ml_543960/fachinformation
7. Carboplatin: http://www.teva.de/index.php?eID=dumpFile&t=f&f=37532&g=-1&r=11068%2C11068&token=eebfb22e78f1cc8d9935d59c087e80630146f49e
8. Epirubicin:
9. Doxorubicin:
10. Liposomales Doxorubicin: https://www.gelbe-liste.de/produkte/Myocet-50-mg-Pulver-Dispersion-u-Loesungsmittel-fuer-ein-Konzentrat-zur-Herstellung-einer-Infusionsdispersion_359323/fachinformation
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12. Mitoxantron: https://www.gelbe-liste.de/produkte/Mitoxantron-Teva-2-mg-ml-Injektionsloesung-15ml_543783/fachinformation
13. Paclitaxel: https://medikamio.com/de-de/medikamente/paclitaxel-ratiopharm/pil
14. Nab-Paclitaxel: https://www.gelbe-liste.de/produkte/Abraxane-5-mg-ml-Pulver-zur-Herstellung-einer-Infusionssuspension_514889/fachinformation
15. Docetaxel: https://mein.sanofi.de/produkte/Taxotere/Downloads?id=89447754-dfb2-450b-b35a-36950de8a74d
16. Vinorelbin: http://www.detect-studien.de/dokumente/d3/fachinfo/Navelbine.pdf
17. Eribulin: http://www.detect-studien.de/dokumente/d4/fachinfo/Fachinfo_Eribulin_Halaven.pdf

<u>Weitere Referenzen (Auswahl)</u>

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2. Petrelli F et al: Mortality, leukemic risk, and cardiovascular toxicity of adjuvant anthracycline and taxane chemotherapy in breast cancer: a meta-analysis. Breast Cancer Res Treat. 2012 Sep;135(2):335-46
3. Jim HS et al: Meta-analysis of cognitive functioning in breast cancer survivors previously treated with standard-dose chemotherapy. J Clin Oncol. 2012 Oct 10;30(29):3578-87
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Onkologie 36(5): 266-272.
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7. Maeda S, Saimura M, Minami S, et al. Efficacy and safety of eribulin as first- to third-line treatment in patients with advanced or metastatic breast cancer previously treated with anthracyclines and taxanes.See comment in PubMed Commons below Breast. 2017 Jan 2;32:66-72. doi: 10.1016/j.breast.2016.12.017.
8. Zhang XH, Hao S, Gao B, et al. A network meta-analysis for toxicity of eight chemotherapy regimens in the treatment of metastatic/advanced breast cancer. Oncotarget. 2016 Dec 20;7(51):84533-84543. doi: 10.18632/oncotarget.13023.
9. Basch E, Prestrud AA, Hesketh PJ, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. Journal of Clinical Oncology 2011;29:4189- 4198
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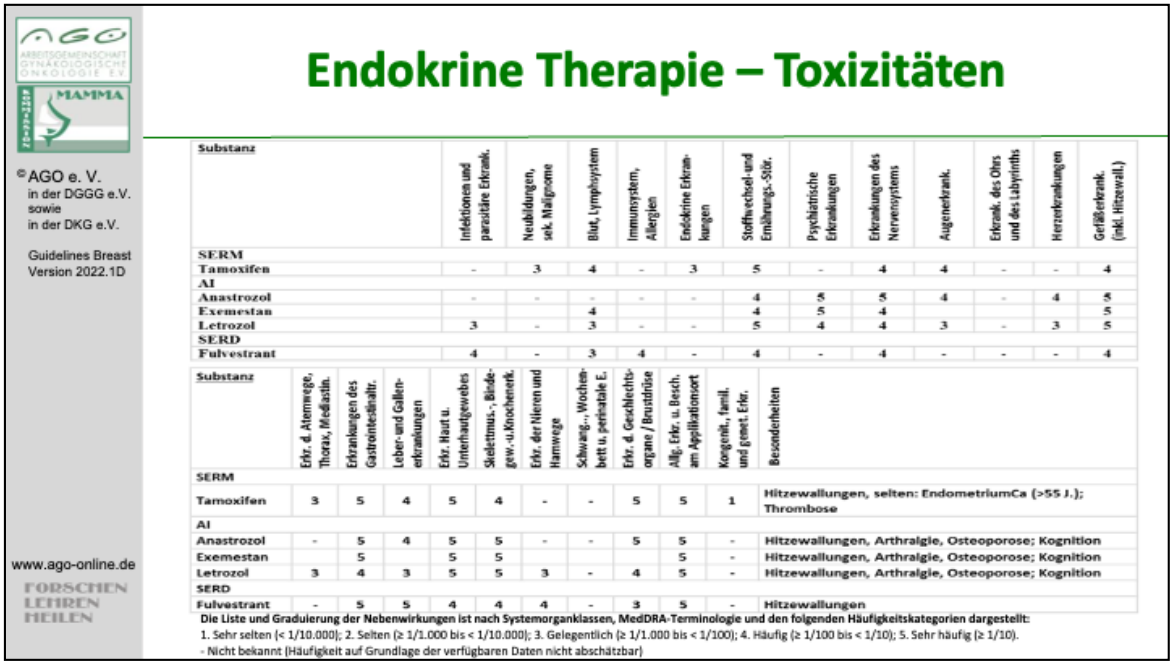

Endokrine Therapie – Toxizitäten

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Guidelines Breast
Version 2022.1D

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FORSCHEN
LEHREN
HEILEN

Substanz	Infektionen und parasitäre Erkrank.	Neubildungen, sek. Malignome	Blut, Lymphsystem	Immunsystem, Allergien	Endokrine Erkrankungen	Stoffwechsel- und Ernährungs-Störungen	Psychiatrische Erkrankungen	Erkrankungen des Nervensystems	Augenerkrank.	Erkrank. des Ohrs und des Labyrinths	Herzerkrankungen	Gefäßerkrank. (inkl. Hitzewall.)
SERM												
Tamoxifen	-	3	4	-	3	5	-	4	4	-	-	4
AI												
Anastrozol	-	-	-	-	-	4	5	5	4	-	4	5
Exemestan			4			4	5	4				5
Letrozol	3	-	3	-	-	5	4	4	3	-	3	5
SERD												
Fulvestrant	4	-	3	4	-	4	-	4	-	-	-	4

Substanz	Erkr. d. Atemwege, Thorax, Mediastin.	Erkrankungen des Gastrointestinaltr.	Leber- und Gallenerkrankungen	Erkr. Haut u. Unterhautgewebes	Skelettmus.-, Bindegew.-u.Knochenerk.	Erkr. der Nieren und Harnwege	Schwang.-, Wochenbett u. perinatale E.	Erkr. d. Geschlechtsorgane / Brustdrüse	Allg. Erkr. u. Besch. am Applikationsort	Kongenit., famil. und genet. Erkr.	Besonderheiten
SERM											
Tamoxifen	3	5	4	5	4	-	-	5	5	1	Hitzewallungen, selten: EndometriumCa (>55 J.); Thrombose
AI											
Anastrozol	-	5	4	5	5	-	-	5	5	-	Hitzewallungen, Arthralgie, Osteoporose; Kognition
Exemestan		5		5	5				5	-	Hitzewallungen, Arthralgie, Osteoporose; Kognition
Letrozol	3	4	3	5	5	3	-	4	5	-	Hitzewallungen, Arthralgie, Osteoporose; Kognition
SERD											
Fulvestrant	-	5	5	4	4	4	-	3	5	-	Hitzewallungen

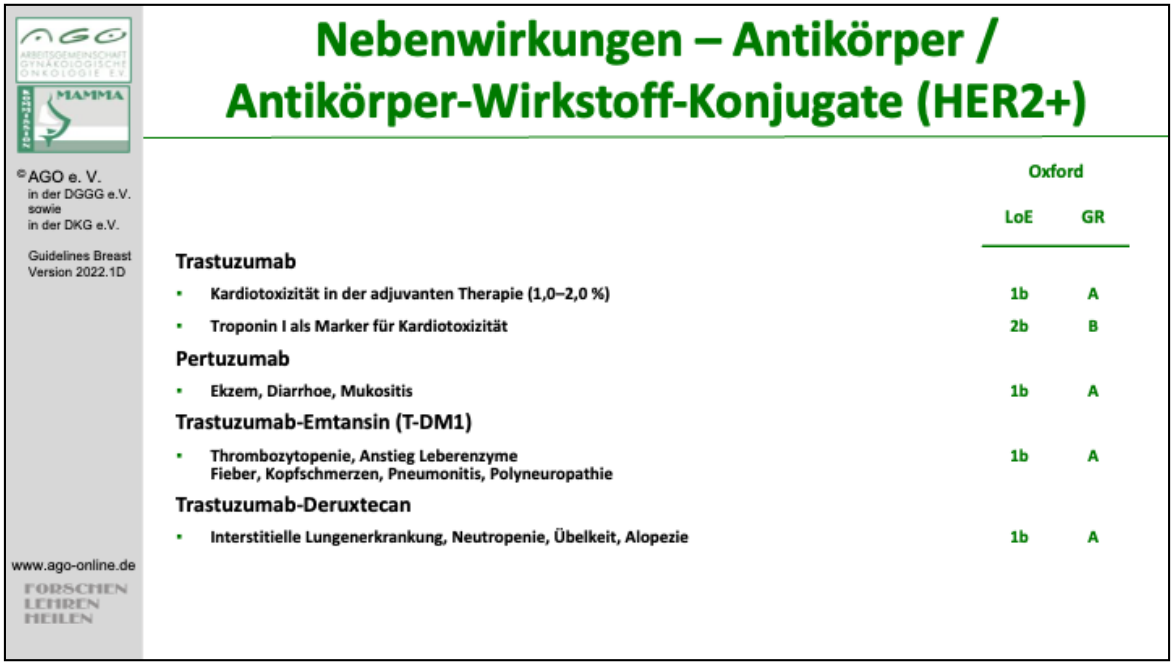
Die Liste und Graduierung der Nebenwirkungen ist nach Systemorganklassen, MedDRA-Terminologie und den folgenden Häufigkeitskategorien dargestellt:
1. Sehr selten (< 1/10.000); 2. Selten (≥ 1/1.000 bis < 1/10.000); 3. Gelegentlich (≥ 1/1.000 bis < 1/100); 4. Häufig (≥ 1/100 bis < 1/10); 5. Sehr häufig (≥ 1/10).
- Nicht bekannt (Häufigkeit auf Grundlage der verfügbaren Daten nicht abschätzbar)

<u>Nebenwirkungskategorien - MedDRA (Medical Dictionary for Regulatory Activities)</u>

1. MedDRA: https://www.meddra.org/ bzw. https://www.meddra.org/sites/default/files/guidance/file/intguide_20_1_english_0.pdf

<u>Quellen für die Fachinformationen (Download 19.01.2018)</u>

1. Tamoxifen: https://www.gelbe-liste.de/produkte/Tamoxifen-20-mg-HEXAL-Filmtbl_8660/fachinformation
2. Anastrozol: https://imedikament.de/anastrozol-ratiopharm-1-mg-filmtabletten/fachinformation
3. Exemestan: http://www.success-studie.de/c/downloads/Fachinfo/FI_ExemestanAromasin.pdf
4. Letrozol: http://www.success-studie.de/b/downloads/Fachinfo/Femara_Juli_2014.pdf
5. Fulvestrant: https://www.gelbe-liste.de/produkte/Fulvestrant-HEXAL-250-mg-Injektionsloesung-in-einer-Fertigspritze_912622/fachinformation



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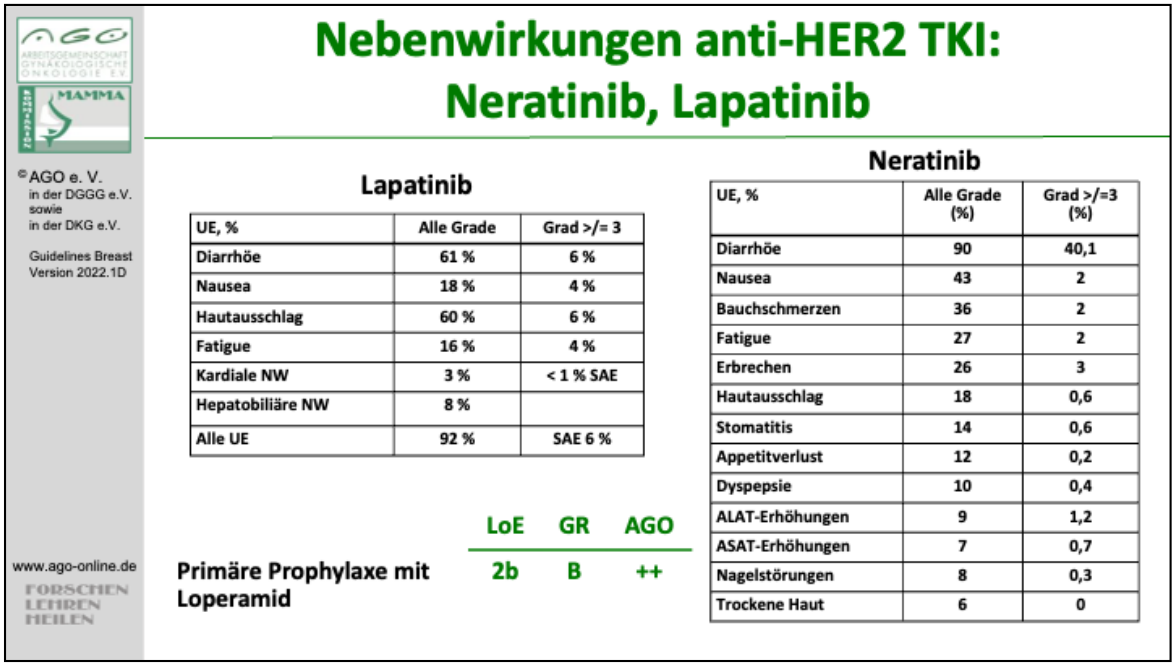

Nebenwirkungen anti-HER2 TKI: Neratinib, Lapatinib

Lapatinib

UE, %	Alle Grade	Grad >/= 3
Diarrhöe	61 %	6 %
Nausea	18 %	4 %
Hautausschlag	60 %	6 %
Fatigue	16 %	4 %
Kardiale NW	3 %	< 1 % SAE
Hepatobiliäre NW	8 %	
Alle UE	92 %	SAE 6 %

	LoE	GR	AGO
Primäre Prophylaxe mit Loperamid	2b	B	++

Neratinib

UE, %	Alle Grade (%)	Grad >/=3 (%)
Diarrhöe	90	40,1
Nausea	43	2
Bauchschmerzen	36	2
Fatigue	27	2
Erbrechen	26	3
Hautausschlag	18	0,6
Stomatitis	14	0,6
Appetitverlust	12	0,2
Dyspepsie	10	0,4
ALAT-Erhöhungen	9	1,2
ASAT-Erhöhungen	7	0,7
Nagelstörungen	8	0,3
Trockene Haut	6	0

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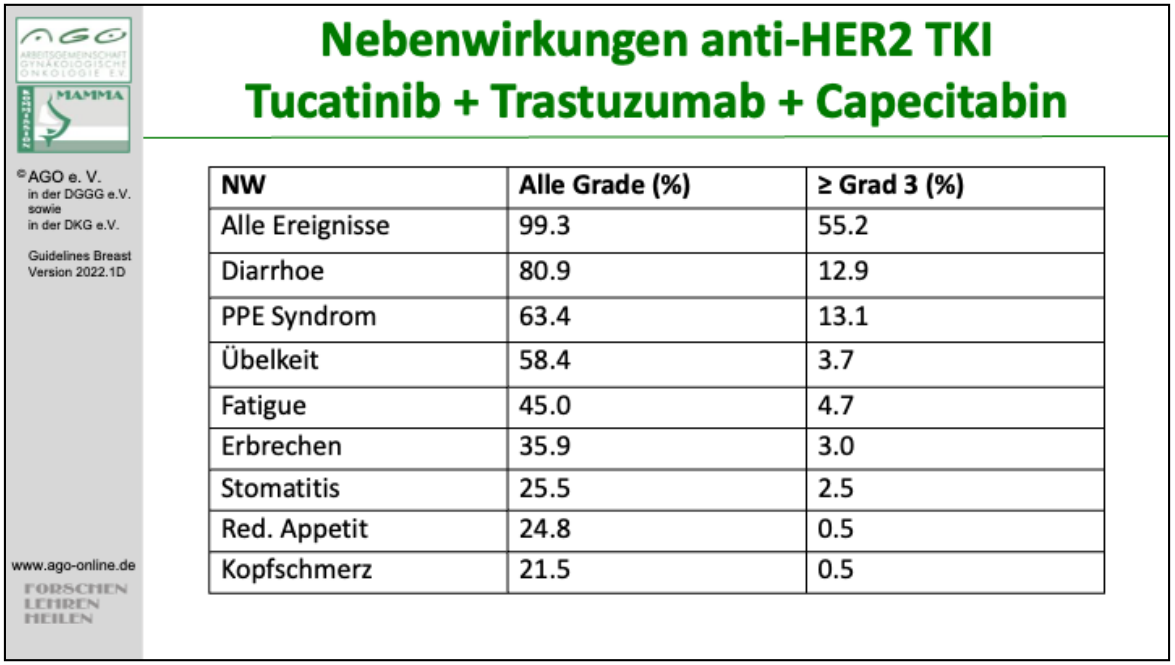

Nebenwirkungen anti-HER2 TKI
Tucatinib + Trastuzumab + Capecitabin

NW	Alle Grade (%)	≥ Grad 3 (%)
Alle Ereignisse	99.3	55.2
Diarrhoe	80.9	12.9
PPE Syndrom	63.4	13.1
Übelkeit	58.4	3.7
Fatigue	45.0	4.7
Erbrechen	35.9	3.0
Stomatitis	25.5	2.5
Red. Appetit	24.8	0.5
Kopfschmerz	21.5	0.5

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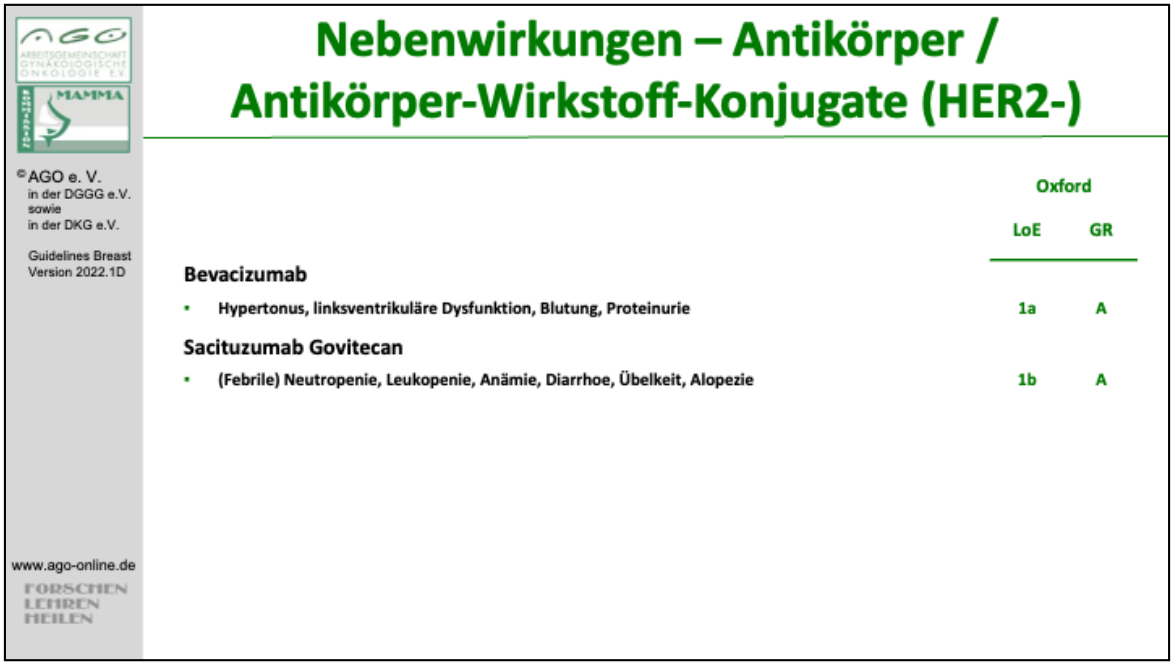

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Sacituzumab Govitecan…

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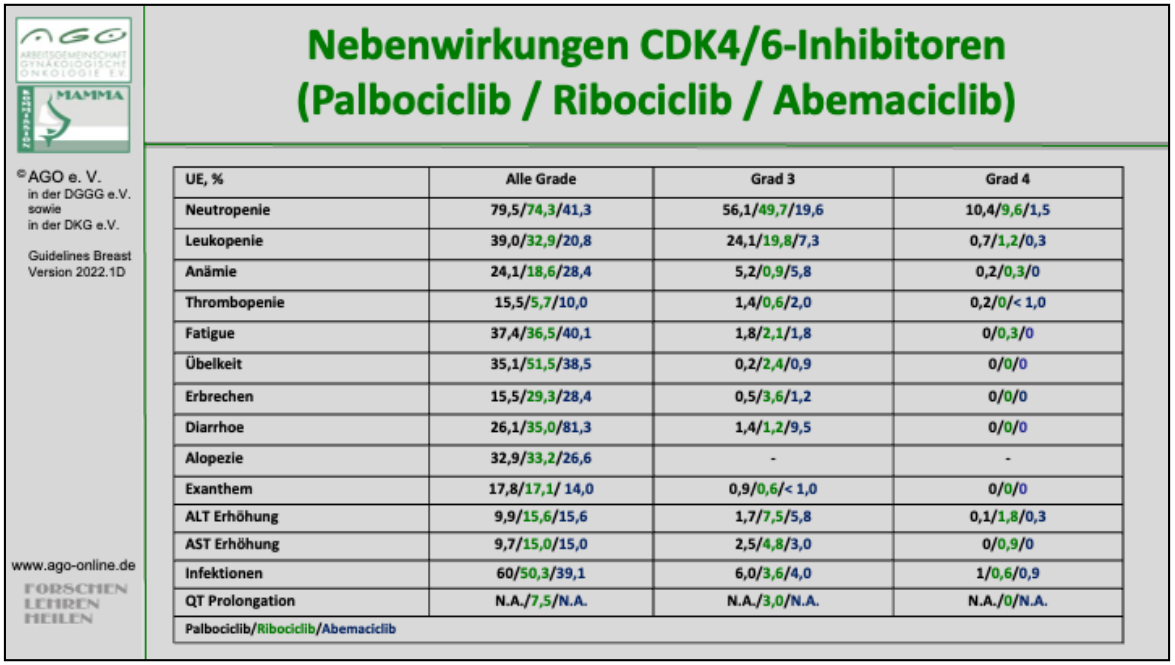

Nebenwirkungen CDK4/6-Inhibitoren (Palbociclib / Ribociclib / Abemaciclib)

UE, %	Alle Grade	Grad 3	Grad 4
Neutropenie	79,5/74,3/41,3	56,1/49,7/19,6	10,4/9,6/1,5
Leukopenie	39,0/32,9/20,8	24,1/19,8/7,3	0,7/1,2/0,3
Anämie	24,1/18,6/28,4	5,2/0,9/5,8	0,2/0,3/0
Thrombopenie	15,5/5,7/10,0	1,4/0,6/2,0	0,2/0/< 1,0
Fatigue	37,4/36,5/40,1	1,8/2,1/1,8	0/0,3/0
Übelkeit	35,1/51,5/38,5	0,2/2,4/0,9	0/0/0
Erbrechen	15,5/29,3/28,4	0,5/3,6/1,2	0/0/0
Diarrhoe	26,1/35,0/81,3	1,4/1,2/9,5	0/0/0
Alopezie	32,9/33,2/26,6	-	-
Exanthem	17,8/17,1/ 14,0	0,9/0,6/< 1,0	0/0/0
ALT Erhöhung	9,9/15,6/15,6	1,7/7,5/5,8	0,1/1,8/0,3
AST Erhöhung	9,7/15,0/15,0	2,5/4,8/3,0	0/0,9/0
Infektionen	60/50,3/39,1	6,0/3,6/4,0	1/0,6/0,9
QT Prolongation	N.A./7,5/N.A.	N.A./3,0/N.A.	N.A./0/N.A.

Palbociclib/Ribociclib/Abemaciclib

Palbociclib

1. Verma S, Bartlett CH, Schnell P, et al. Palbociclib in Combination With Fulvestrant in Women With Hormone Receptor-Positive/HER2-Negative Advanced Metastatic Breast Cancer: Detailed Safety Analysis From a Multicenter, Randomized, Placebo-Controlled, Phase III Study (PALOMA-3). Oncologist. 2016 Oct;21(10):1165-1175. Epub 2016 Jul 1.
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Ribociclib

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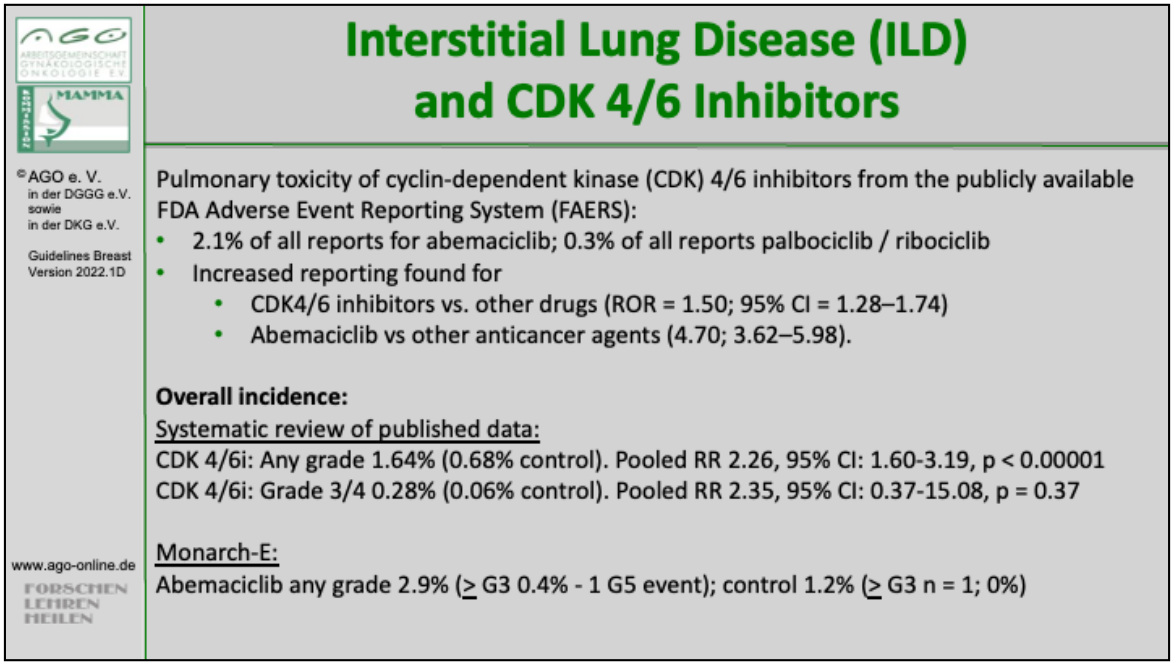

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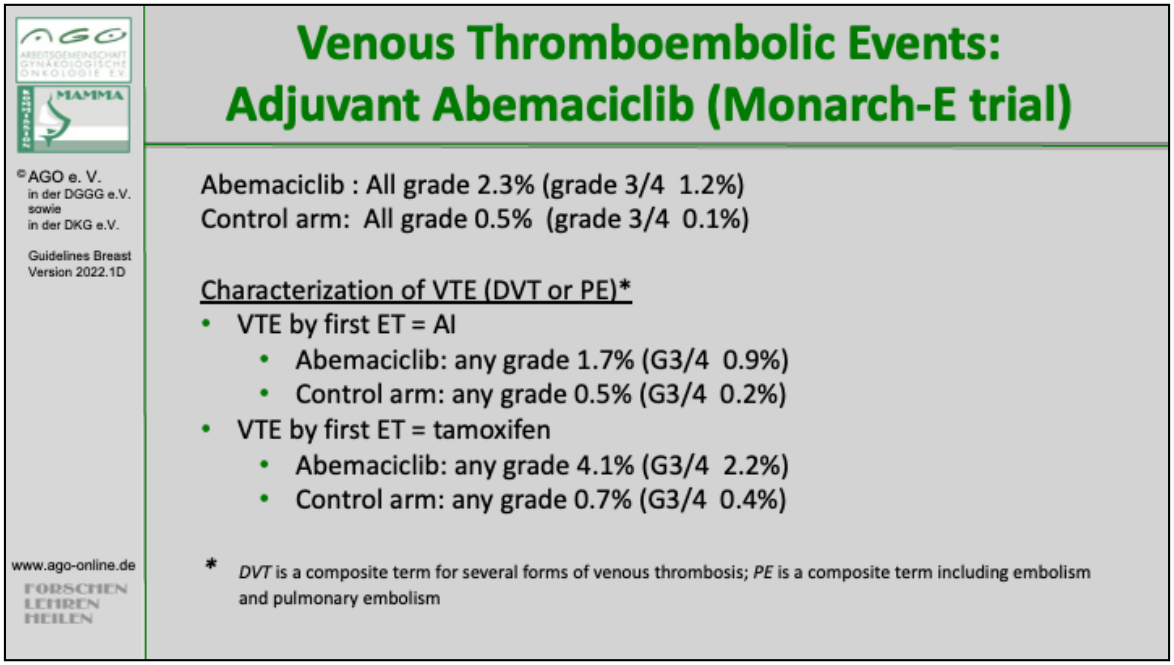

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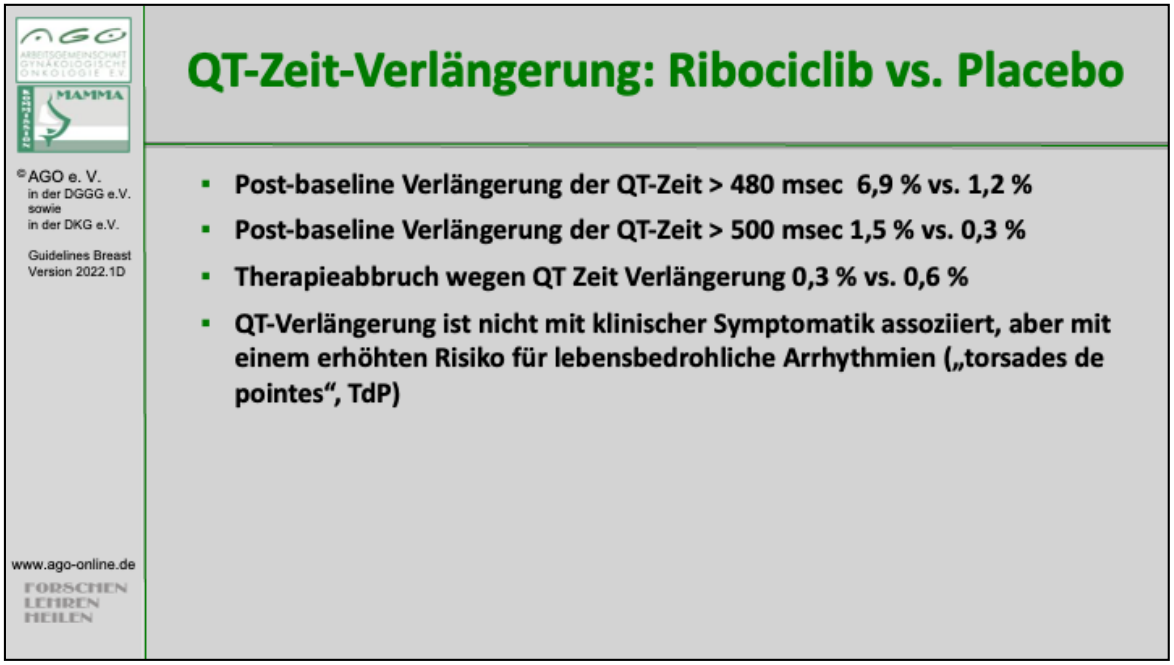

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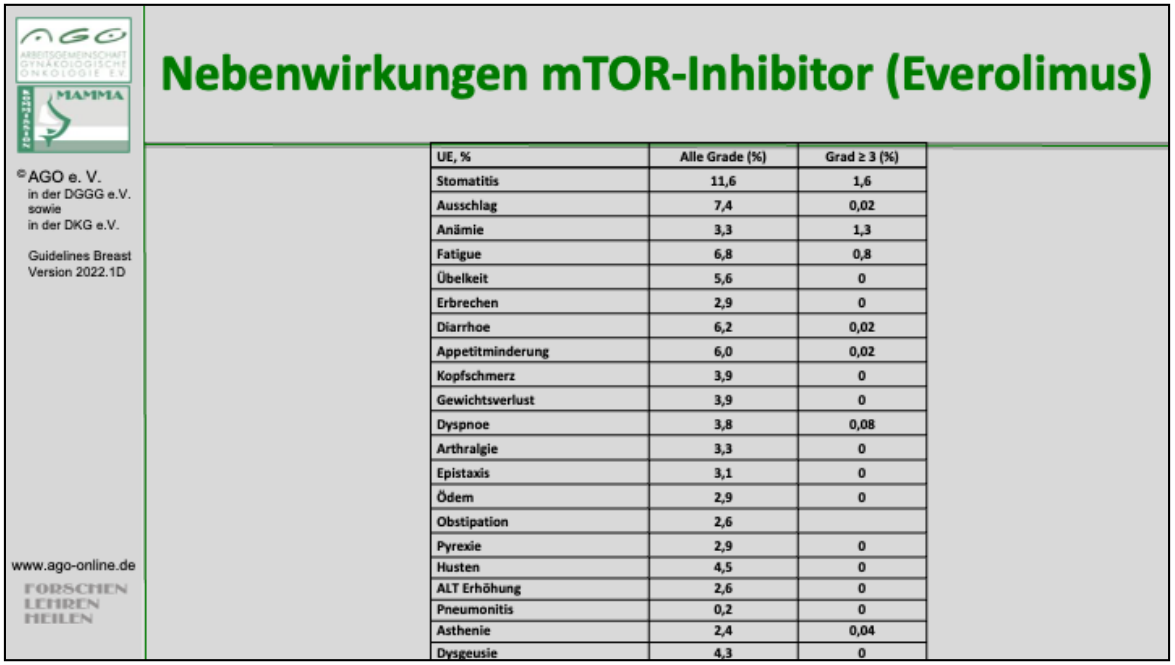
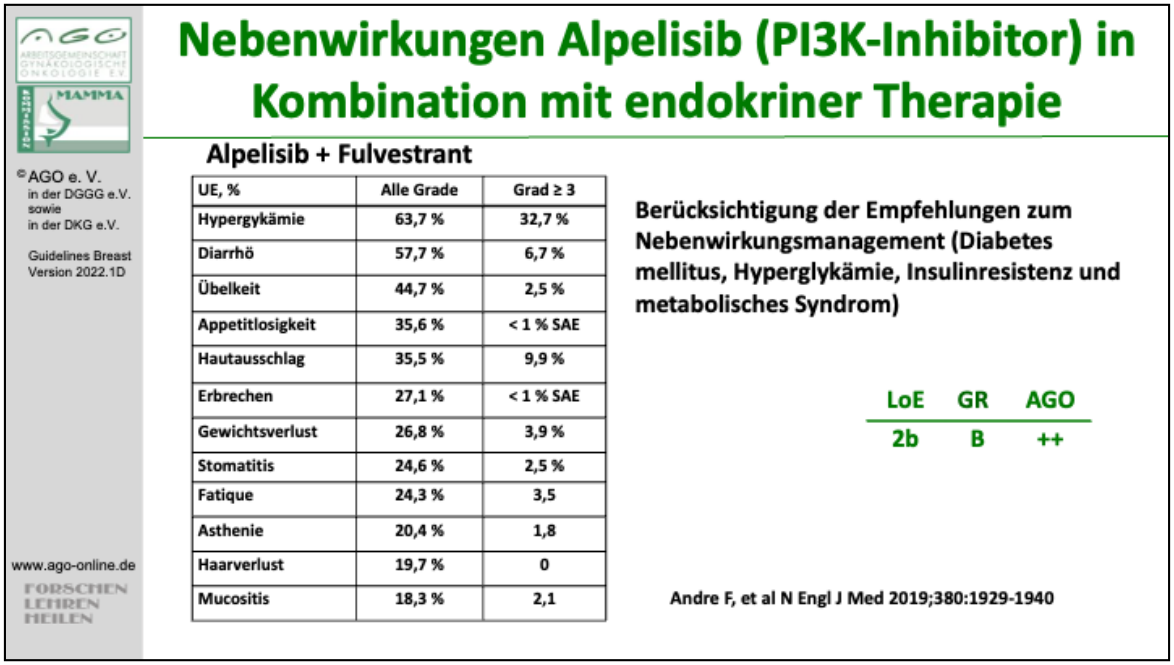


UE, %	Alle Grade (%)	Grad ≥ 3 (%)
Stomatitis	11,6	1,6
Ausschlag	7,4	0,02
Anämie	3,3	1,3
Fatigue	6,8	0,8
Übelkeit	5,6	0
Erbrechen	2,9	0
Diarrhoe	6,2	0,02
Appetitminderung	6,0	0,02
Kopfschmerz	3,9	0
Gewichtsverlust	3,9	0
Dyspnoe	3,8	0,08
Arthralgie	3,3	0
Epistaxis	3,1	0
Ödem	2,9	0
Obstipation	2,6	
Pyrexie	2,9	0
Husten	4,5	0
ALT Erhöhung	2,6	0
Pneumonitis	0,2	0
Asthenie	2,4	0,04
Dysgeusie	4,3	0

1. Baselga J, Campone M, Piccart M et al Everolimus in postmenopausal hormone receptor-positive advanced breast cancer N Engl J Med 2012; 366: 520-529.



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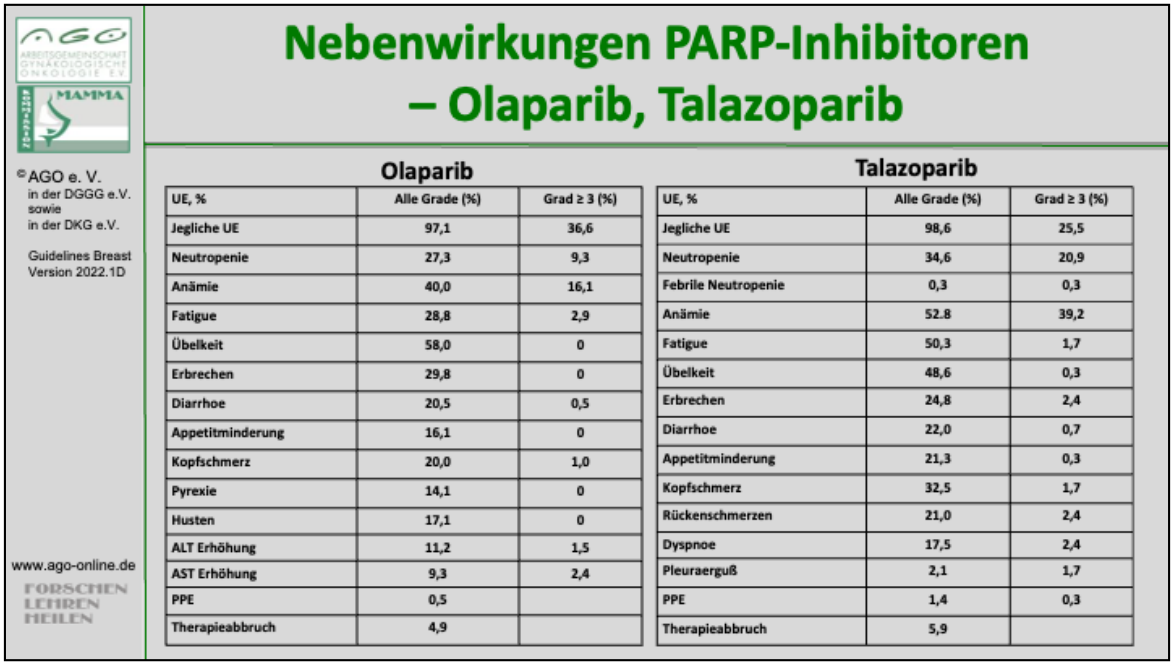

Olaparib

UE, %	Alle Grade (%)	Grad ≥ 3 (%)
Jegliche UE	97,1	36,6
Neutropenie	27,3	9,3
Anämie	40,0	16,1
Fatigue	28,8	2,9
Übelkeit	58,0	0
Erbrechen	29,8	0
Diarrhoe	20,5	0,5
Appetitminderung	16,1	0
Kopfschmerz	20,0	1,0
Pyrexie	14,1	0
Husten	17,1	0
ALT Erhöhung	11,2	1,5
AST Erhöhung	9,3	2,4
PPE	0,5	
Therapieabbruch	4,9	

Talazoparib

UE, %	Alle Grade (%)	Grad ≥ 3 (%)
Jegliche UE	98,6	25,5
Neutropenie	34,6	20,9
Febrile Neutropenie	0,3	0,3
Anämie	52.8	39,2
Fatigue	50,3	1,7
Übelkeit	48,6	0,3
Erbrechen	24,8	2,4
Diarrhoe	22,0	0,7
Appetitminderung	21,3	0,3
Kopfschmerz	32,5	1,7
Rückenschmerzen	21,0	2,4
Dyspnoe	17,5	2,4
Pleuraerguß	2,1	1,7
PPE	1,4	0,3
Therapieabbruch	5,9	

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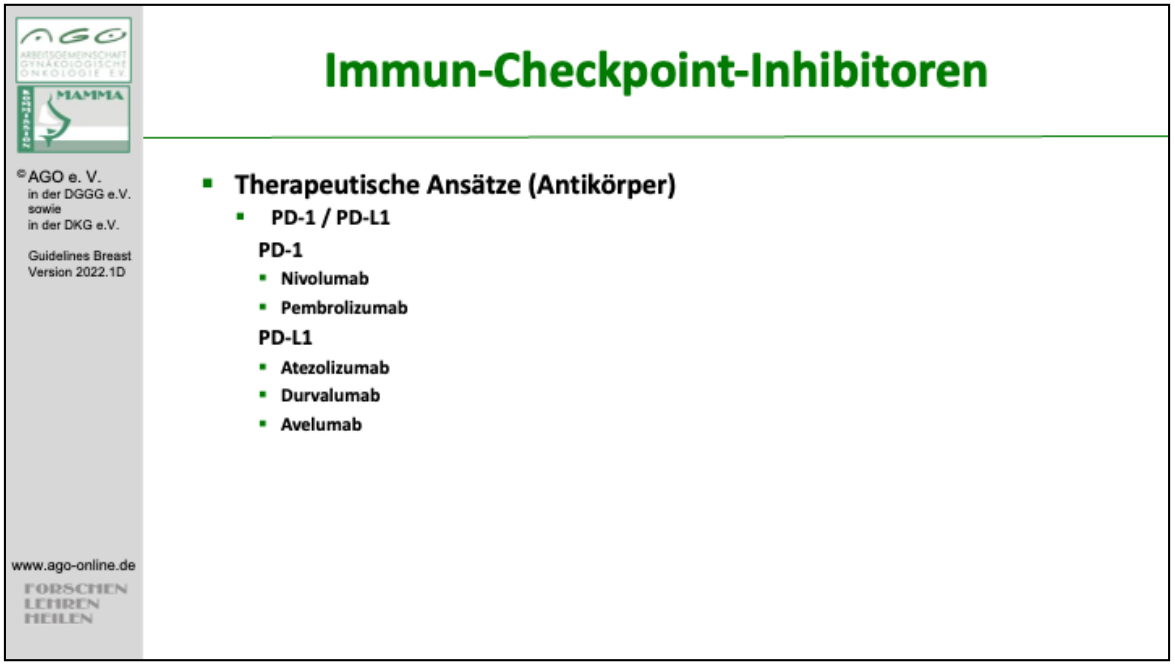

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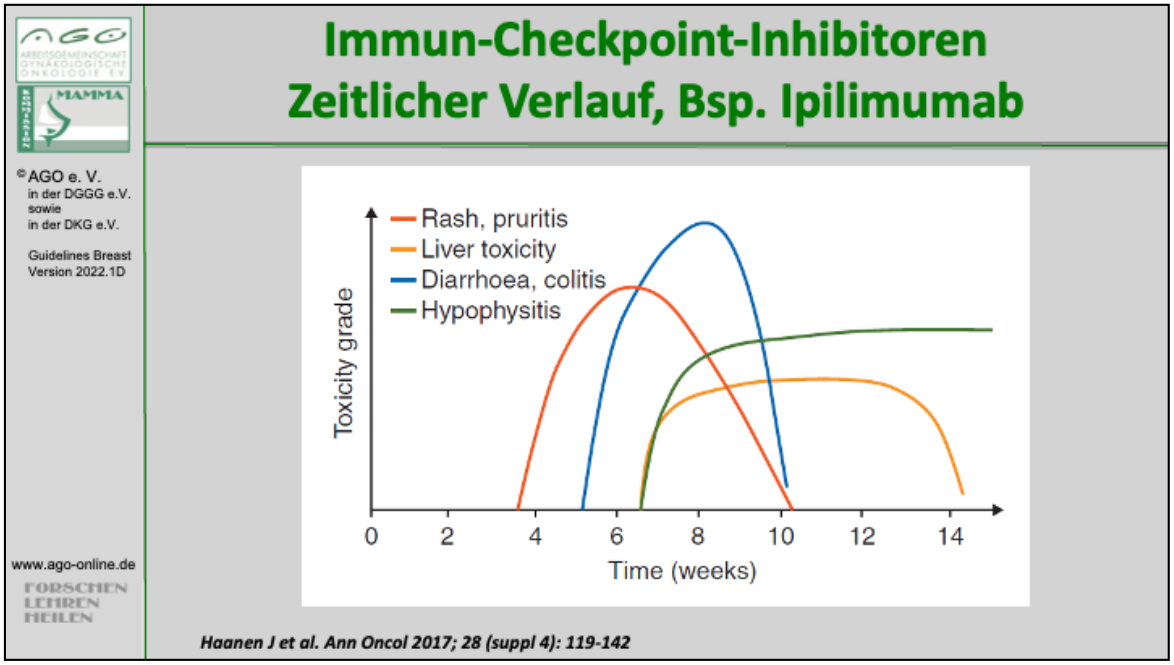

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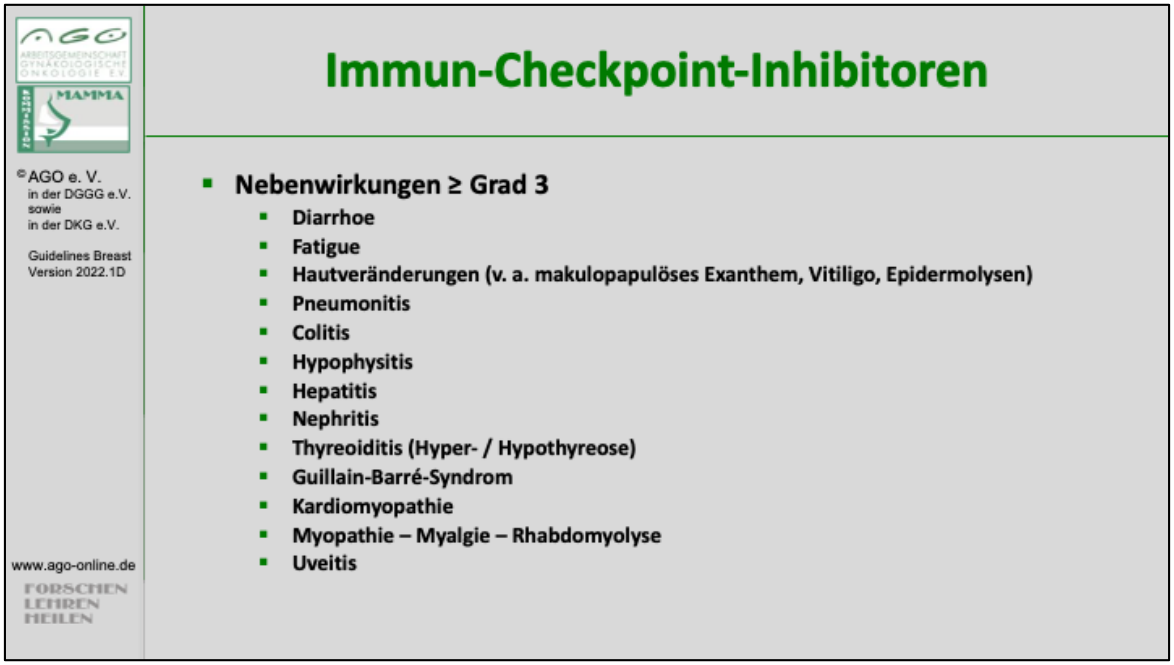

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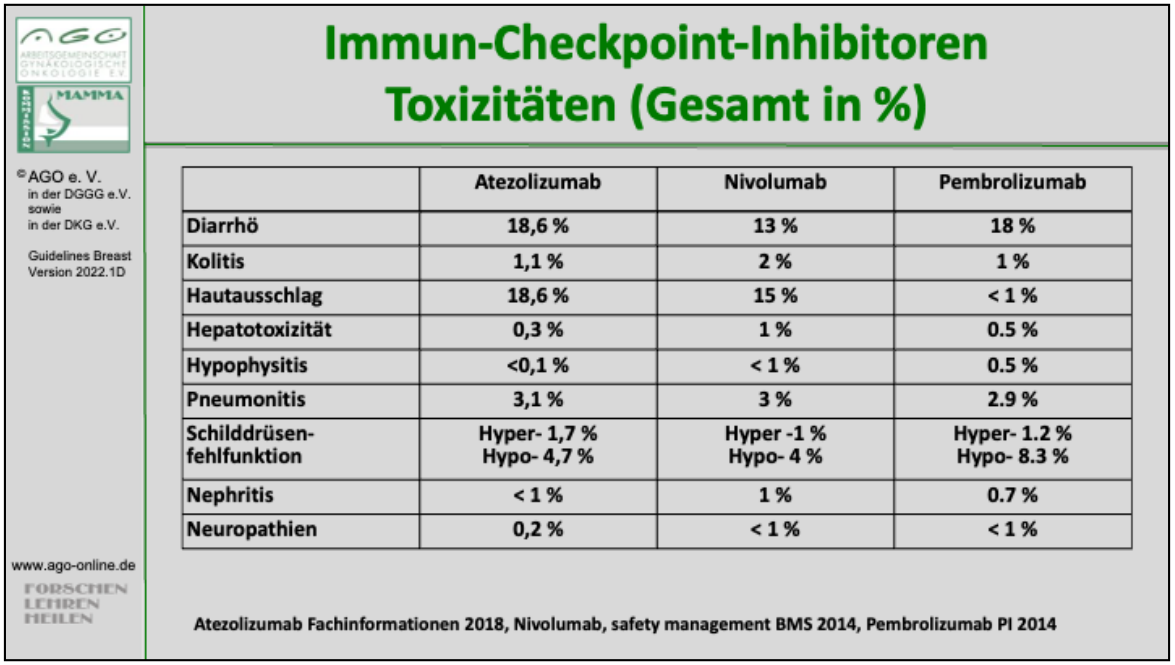
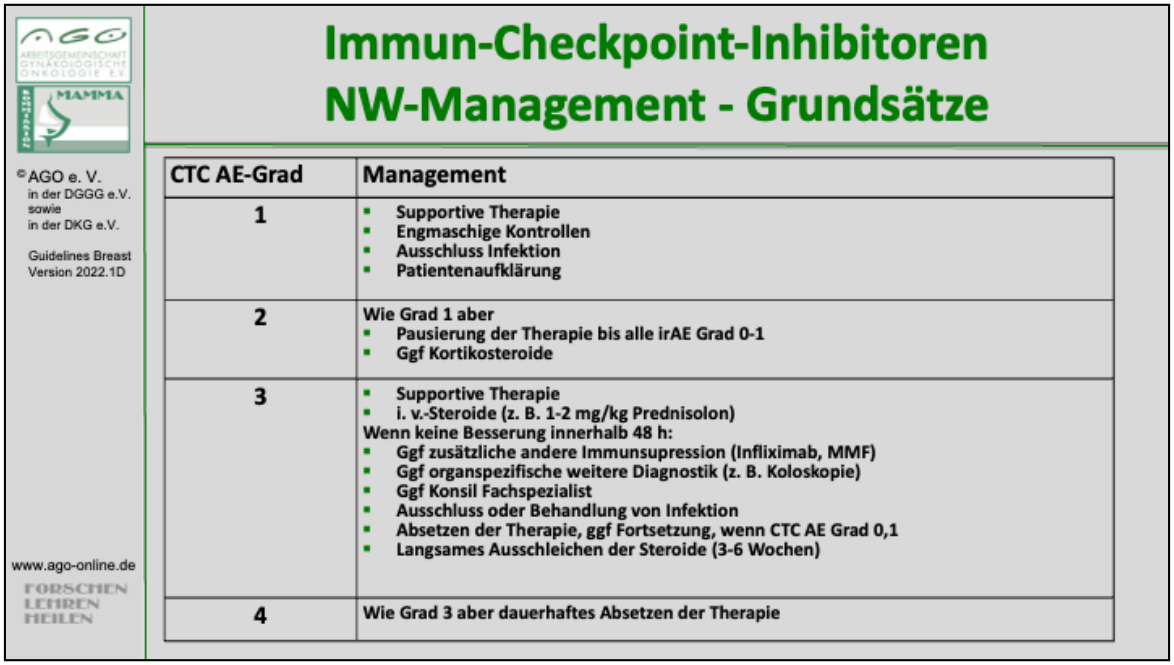


Immun-Checkpoint-Inhibitoren Toxizitäten (Gesamt in %)

	Atezolizumab	Nivolumab	Pembrolizumab
Diarrhö	18,6 %	13 %	18 %
Kolitis	1,1 %	2 %	1 %
Hautausschlag	18,6 %	15 %	< 1 %
Hepatotoxizität	0,3 %	1 %	0.5 %
Hypophysitis	<0,1 %	< 1 %	0.5 %
Pneumonitis	3,1 %	3 %	2.9 %
Schilddrüsen-fehlfunktion	Hyper- 1,7 % Hypo- 4,7 %	Hyper -1 % Hypo- 4 %	Hyper- 1.2 % Hypo- 8.3 %
Nephritis	< 1 %	1 %	0.7 %
Neuropathien	0,2 %	< 1 %	< 1 %

Atezolizumab Fachinformationen 2018, Nivolumab, safety management BMS 2014, Pembrolizumab PI 2014

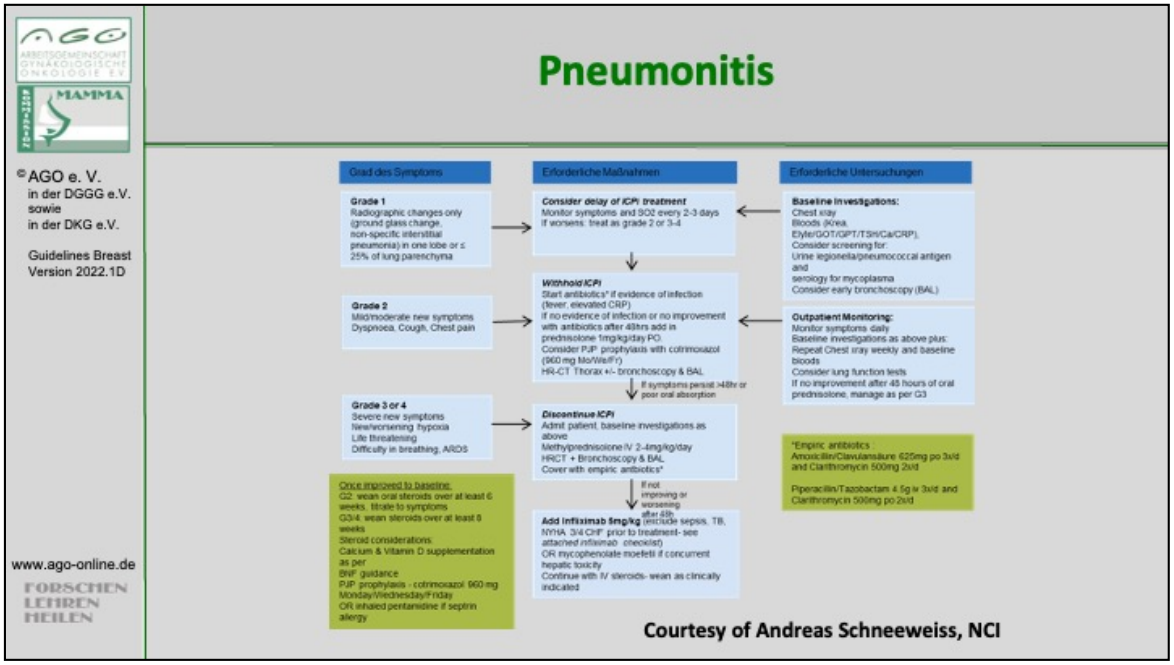
1. Atezolizumab: https://www.fachinfo.de/suche/fi/021700
2. Nivolumab: https://www.fachinfo.de/suche/fi/020675
3. Pembrolizumab: https://www.fachinfo.de/suche/fi/020716



Immun-Checkpoint-Inhibitoren
NW-Management - Grundsätze

CTC AE-Grad	Management
1	▪ Supportive Therapie ▪ Engmaschige Kontrollen ▪ Ausschluss Infektion ▪ Patientenaufklärung
2	Wie Grad 1 aber ▪ Pausierung der Therapie bis alle irAE Grad 0-1 ▪ Ggf Kortikosteroide
3	▪ Supportive Therapie ▪ i. v.-Steroide (z. B. 1-2 mg/kg Prednisolon) Wenn keine Besserung innerhalb 48 h: ▪ Ggf zusätzliche andere Immunsupression (Infliximab, MMF) ▪ Ggf organspezifische weitere Diagnostik (z. B. Koloskopie) ▪ Ggf Konsil Fachspezialist ▪ Ausschluss oder Behandlung von Infektion ▪ Absetzen der Therapie, ggf Fortsetzung, wenn CTC AE Grad 0,1 ▪ Langsames Ausschleichen der Steroide (3-6 Wochen)
4	Wie Grad 3 aber dauerhaftes Absetzen der Therapie

1. Haanen J, Carbonnel F, Robert C, et al. on behalf of the ESMO Guidelines Committee: Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017; 28 (suppl 4): 119-142.



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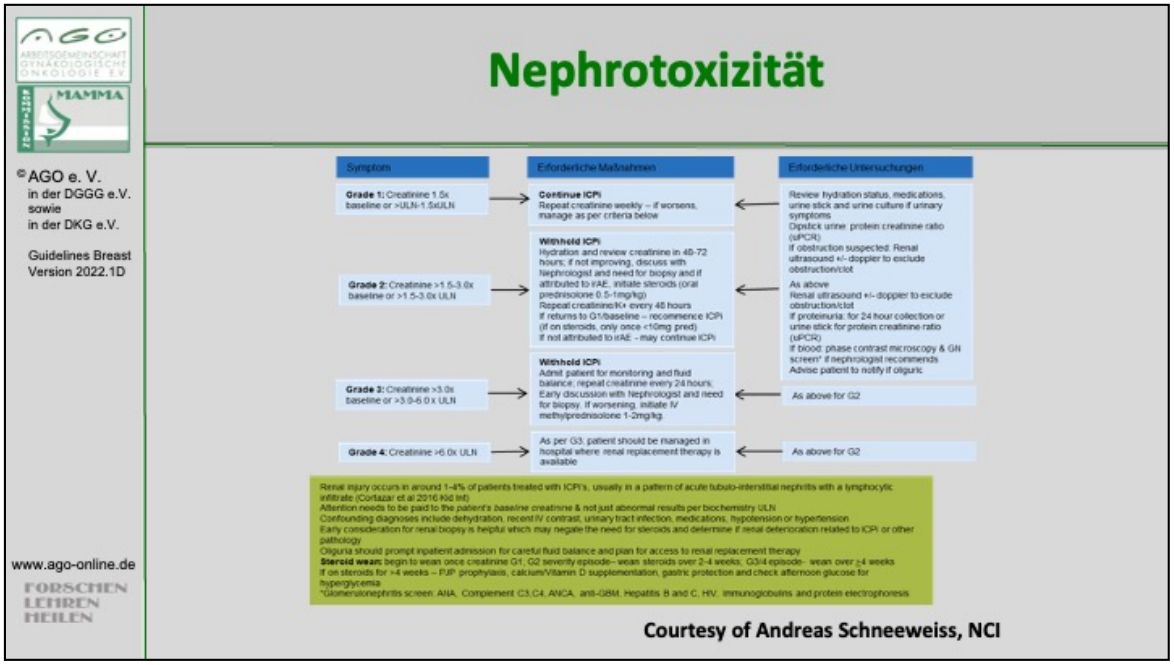

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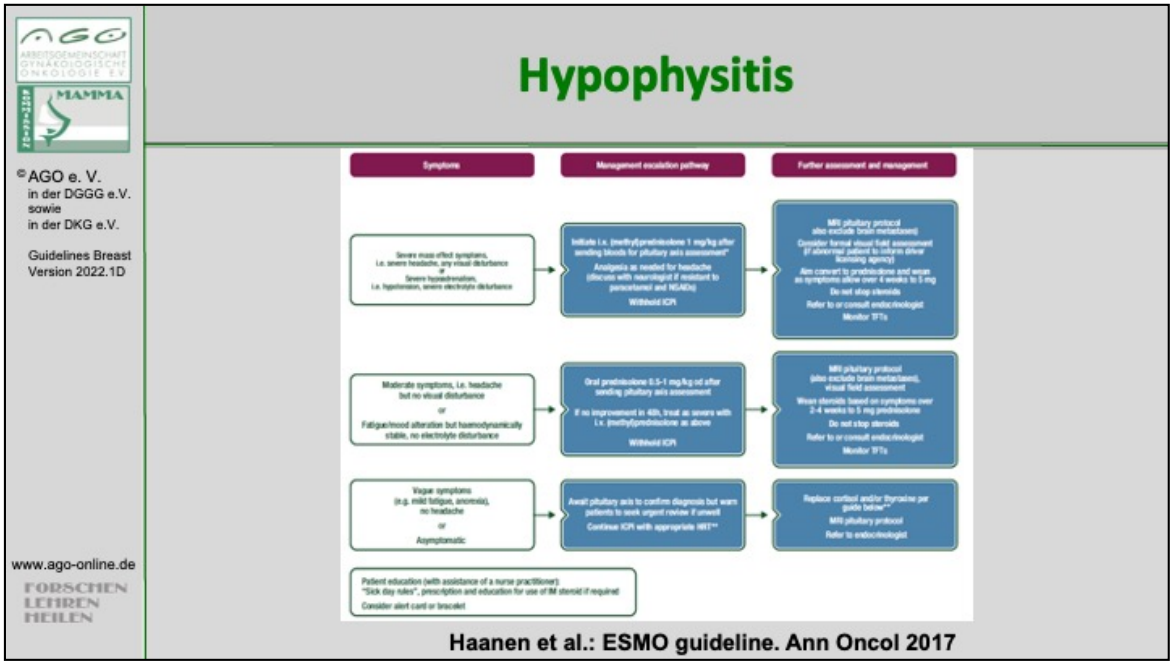

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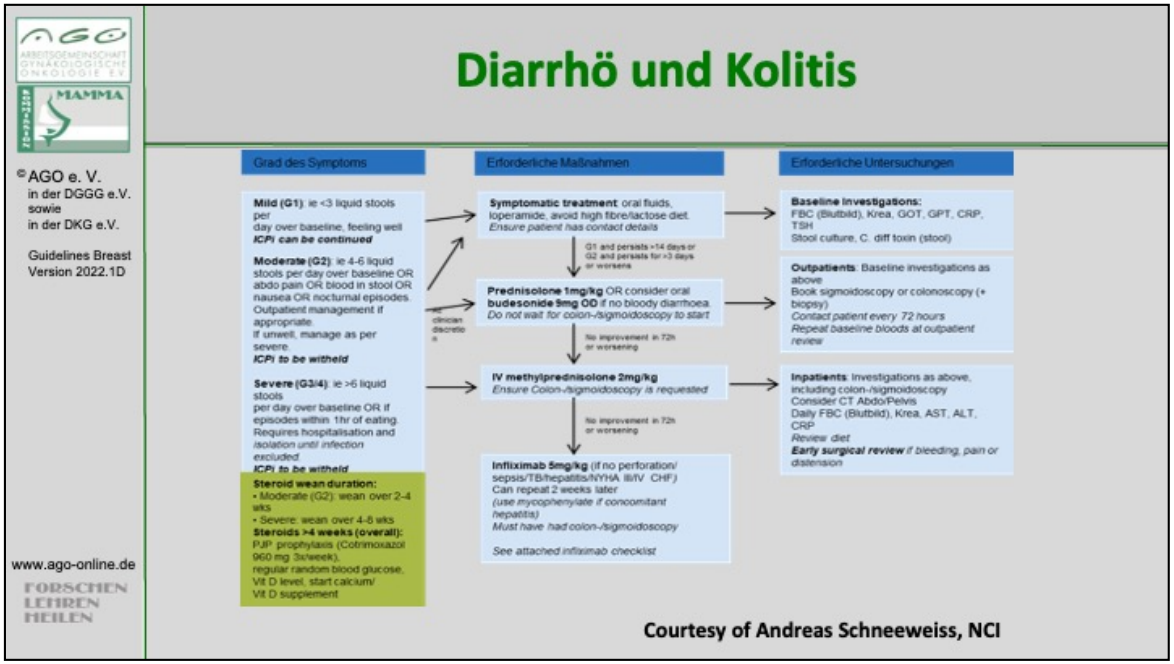

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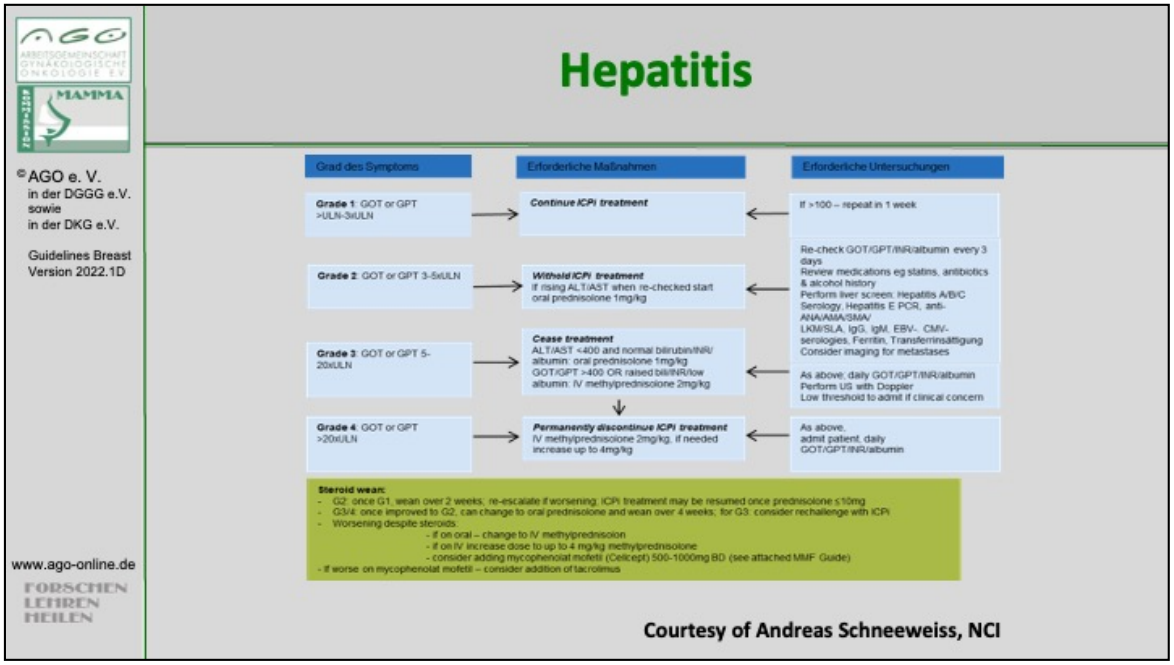

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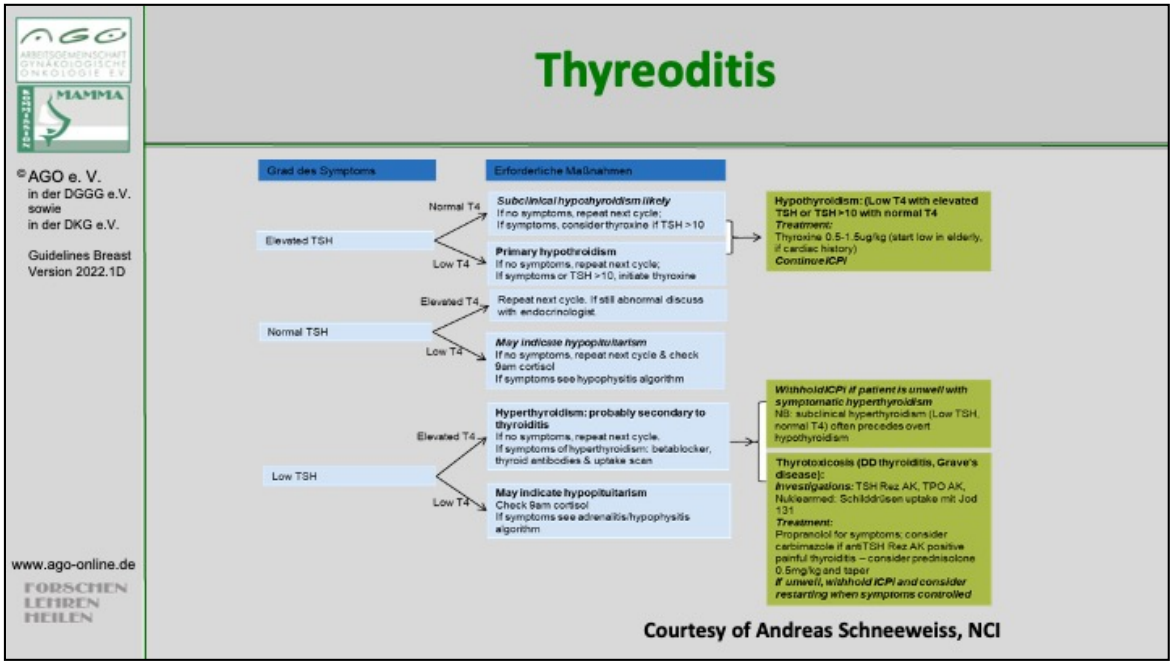

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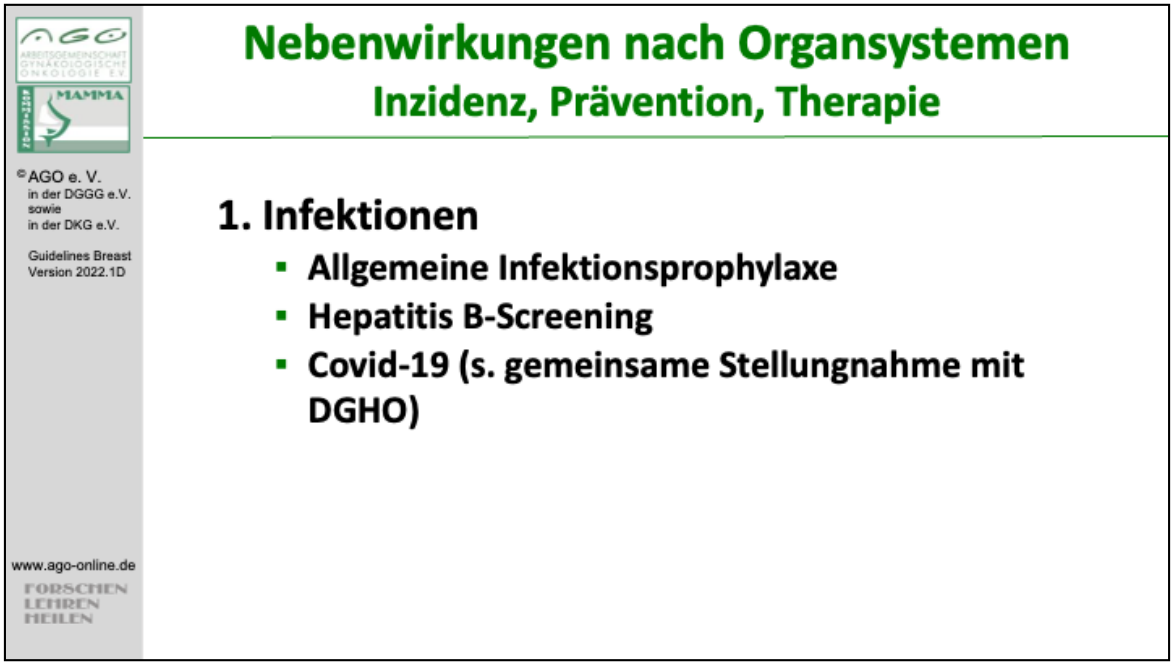

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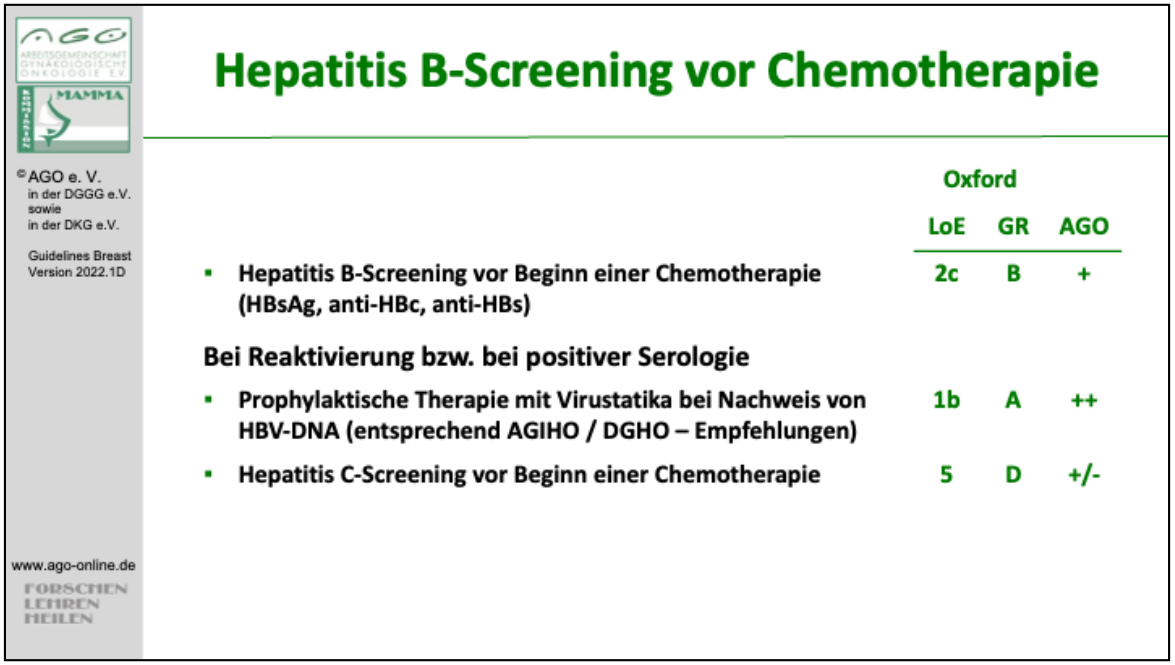

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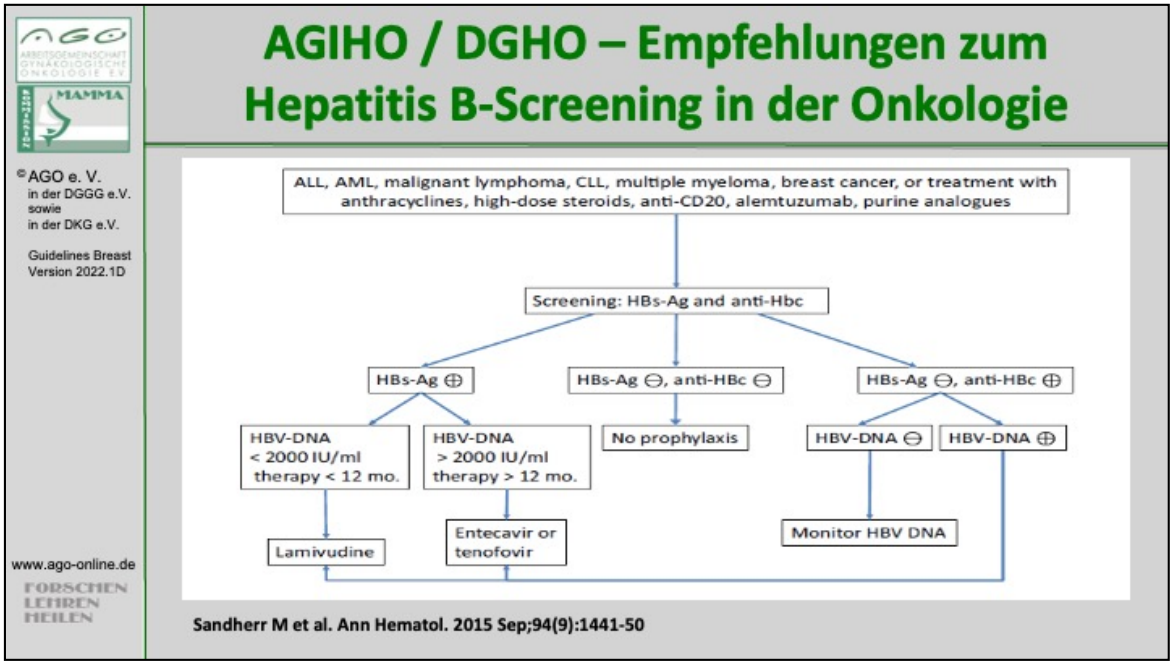

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Guidelines Breast
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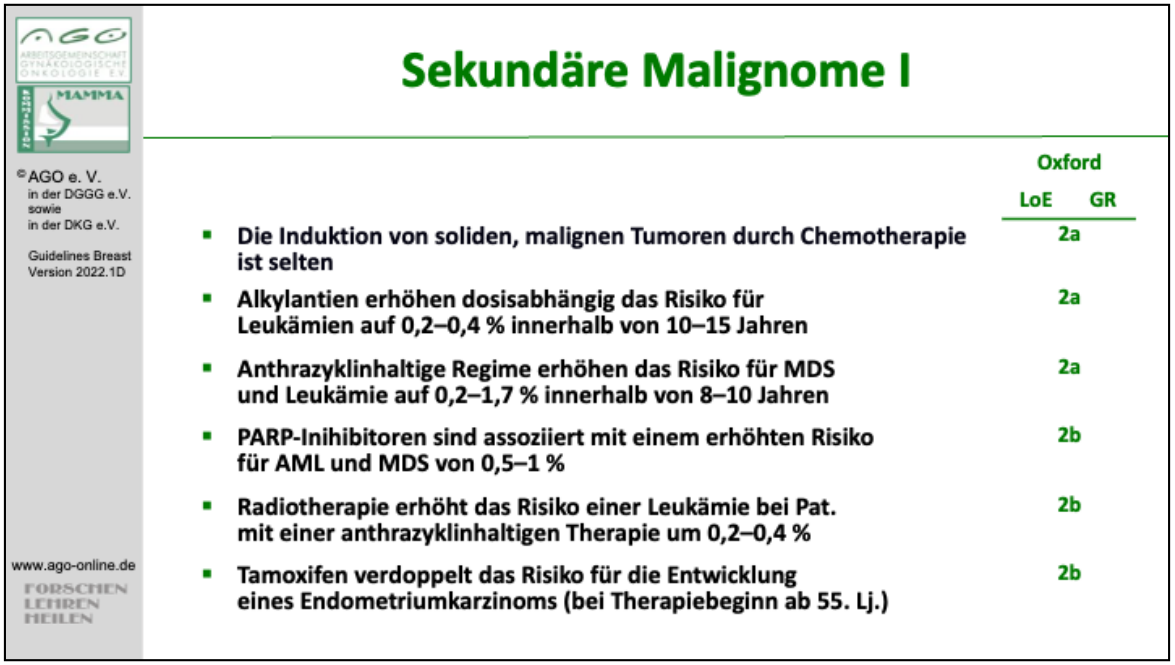
FORSCHEN
LEHREN
HEILEN

Nebenwirkungen nach Organsystemen

Inzidenz, Prävention, Therapie

2. Gutartige, bösartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen)



Statements 1-4

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Tamoxifen and endometrial cancer

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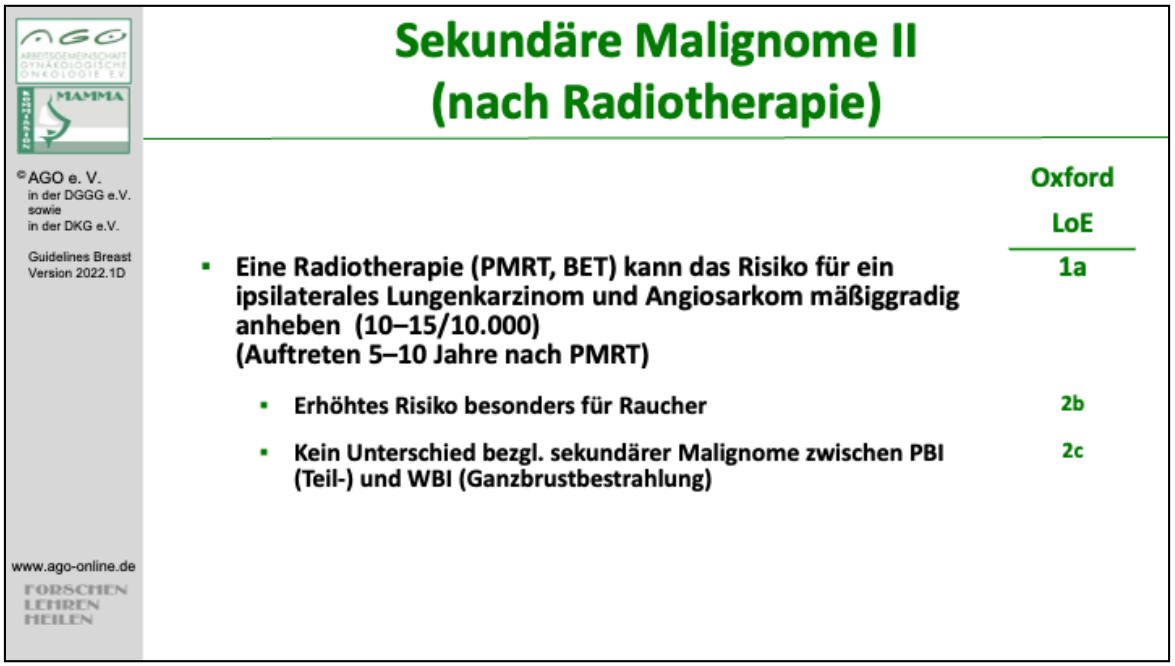

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Guidelines Breast
Version 2022.1D

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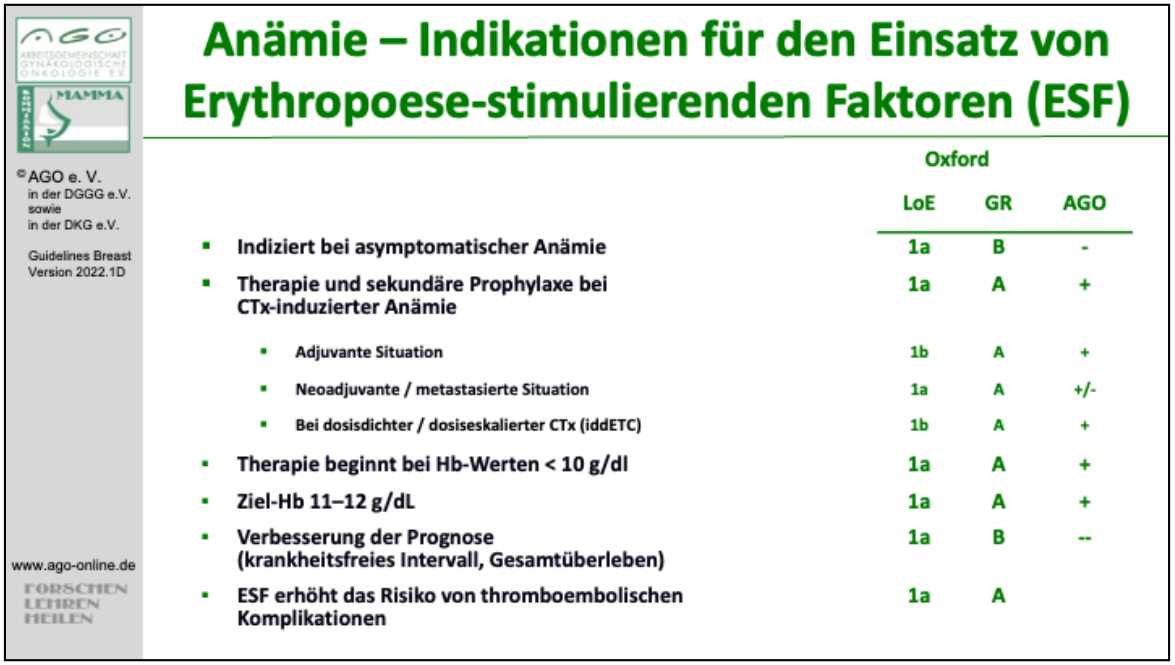
FORSCHEN
LEHREN
HEILEN

Nebenwirkungen nach Organsystemen

Inzidenz, Prävention, Therapie

3. **Erkrankungen des Blutes und des Lymphsystems**
   - **Anämie**
   - **Neutropenie**
   - **Febrile Neutropenie**



Anämie – Indikationen für den Einsatz von Erythropoese-stimulierenden Faktoren (ESF)

	Oxford		
	LoE	GR	AGO
▪ Indiziert bei asymptomatischer Anämie	1a	B	-
▪ Therapie und sekundäre Prophylaxe bei CTx-induzierter Anämie	1a	A	+
▪ Adjuvante Situation	1b	A	+
▪ Neoadjuvante / metastasierte Situation	1a	A	+/-
▪ Bei dosisdichter / dosiseskalierter CTx (iddETC)	1b	A	+
▪ Therapie beginnt bei Hb-Werten < 10 g/dl	1a	A	+
▪ Ziel-Hb 11–12 g/dL	1a	A	+
▪ Verbesserung der Prognose (krankheitsfreies Intervall, Gesamtüberleben)	1a	B	--
▪ ESF erhöht das Risiko von thromboembolischen Komplikationen	1a	A	

Leitlinie:

Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3, 2020,
AWMF Registernummer: 032/054OL

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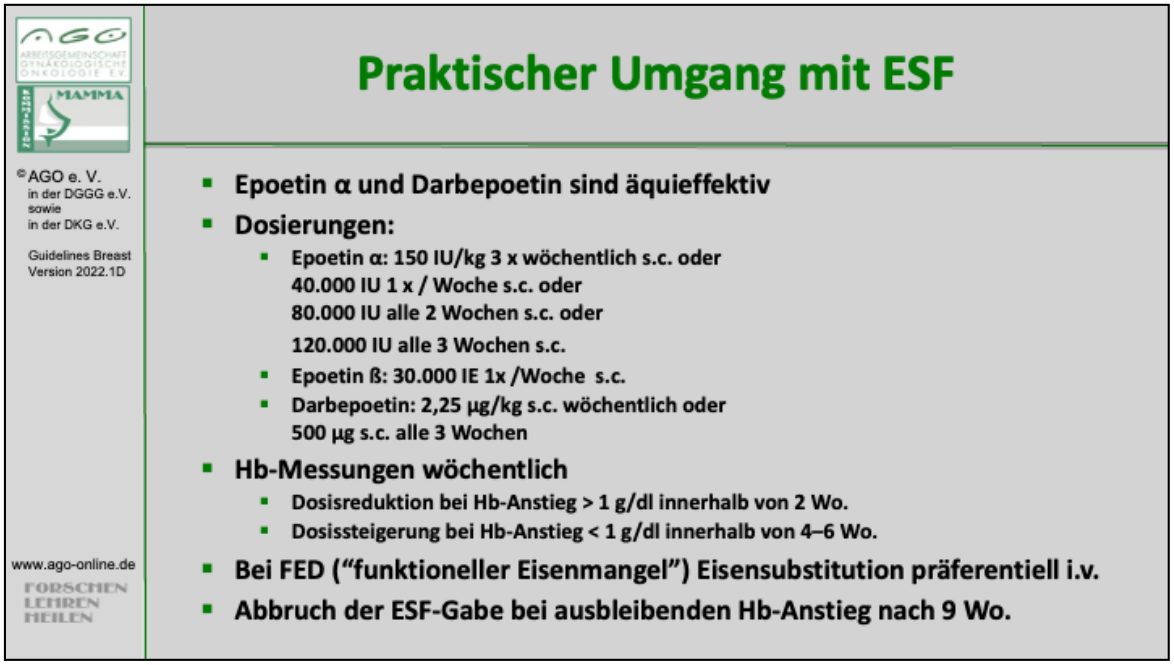

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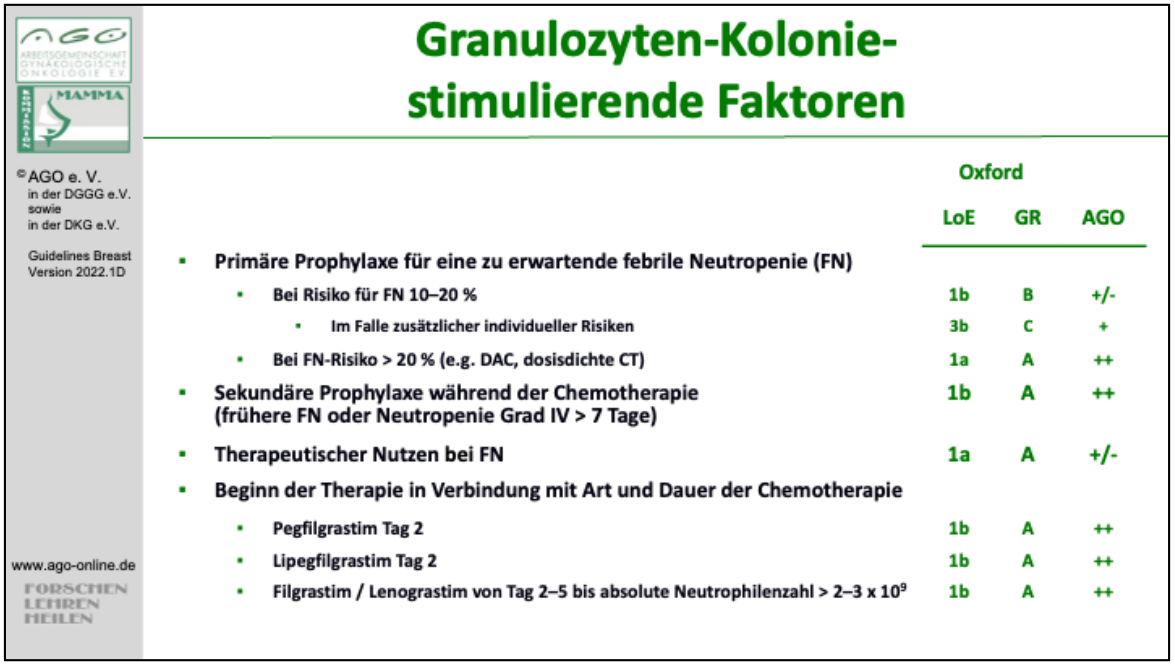

Granulozyten-Kolonie-stimulierende Faktoren

	Oxford LoE	Oxford GR	AGO
▪ **Primäre Prophylaxe für eine zu erwartende febrile Neutropenie (FN)**			
▪ Bei Risiko für FN 10–20 %	1b	B	+/-
▪ Im Falle zusätzlicher individueller Risiken	3b	C	+
▪ Bei FN-Risiko > 20 % (e.g. DAC, dosisdichte CT)	1a	A	++
▪ **Sekundäre Prophylaxe während der Chemotherapie (frühere FN oder Neutropenie Grad IV > 7 Tage)**	1b	A	++
▪ **Therapeutischer Nutzen bei FN**	1a	A	+/-
▪ **Beginn der Therapie in Verbindung mit Art und Dauer der Chemotherapie**			
▪ Pegfilgrastim Tag 2	1b	A	++
▪ Lipegfilgrastim Tag 2	1b	A	++
▪ Filgrastim / Lenograstim von Tag 2–5 bis absolute Neutrophilenzahl > 2–3 x 10^9	1b	A	++

Relevante Leitlinien

1. S3-Leitlinie: Supportive Therapie:
   Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3 – Februar 2020
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Management der febrilen Neutropenie

Arbeitsgemeinschaft Infektionen in der Hämatologie und Onkologie (AGIHO)
der Deutschen Gesellschaft für Hämatologie und Onkologie e.V. (DGHO) www.dgho-infektionen.de

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Definition (orale Temp. > 38,5 °C oder zwei konsekutive Messungen > 38 °C über 2 h in einer Patientin mit einem ANC < 500 cells/mm³ oder erwarteter Abfall < 500 cells/mm³)

	Oxford		
	LoE	GR	AGO
▪ Klinische Untersuchung	5	D	++
▪ Tägliche Kontrollen	5	D	++
▪ Hospitalisierung von Hochrisikopatienten	1b	A	++
▪ Ambulante Therapie bei Niedrigrisikopat. möglich	1b	A	+
▪ Differentialblutbild	5	D	++
▪ Blutkulturen	5	D	++
▪ Bildgebung der Lunge	3	C	++
▪ Sofortige empirische antibiot. Therapie	1a	A	++
▪ Empirische antimykotische Therapie nach 4–7 d bei keiner Besserung unter der antibiotischen Therapie	1b	A	++
▪ G-CSF als therapeutische Maßnahme	2b	B	+/-

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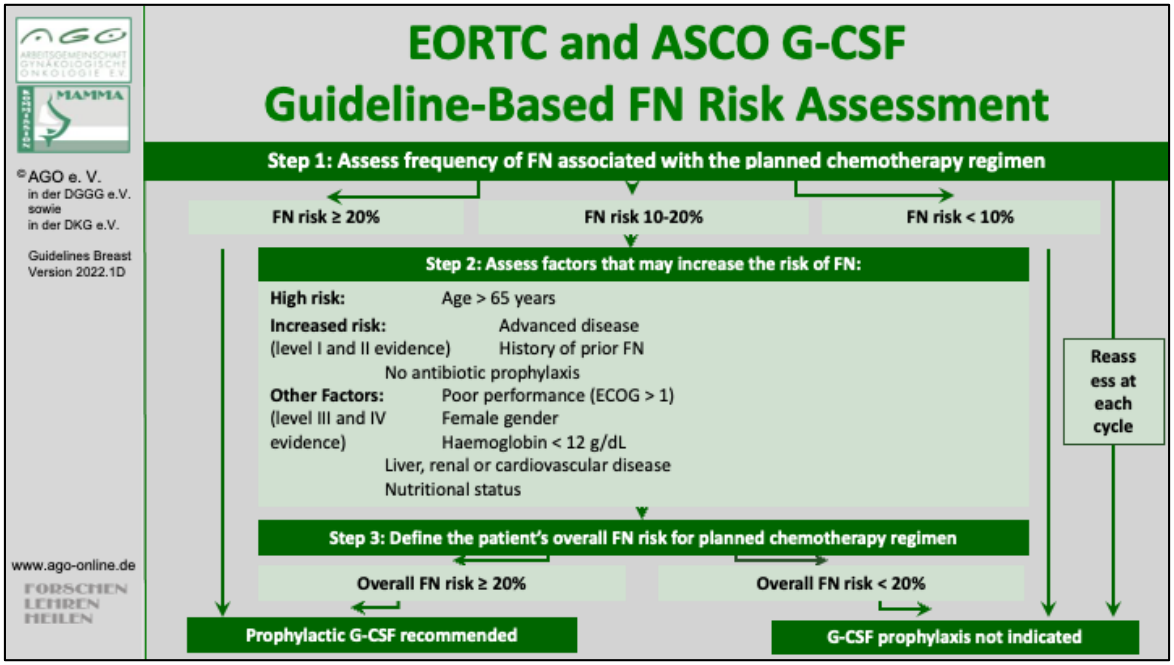

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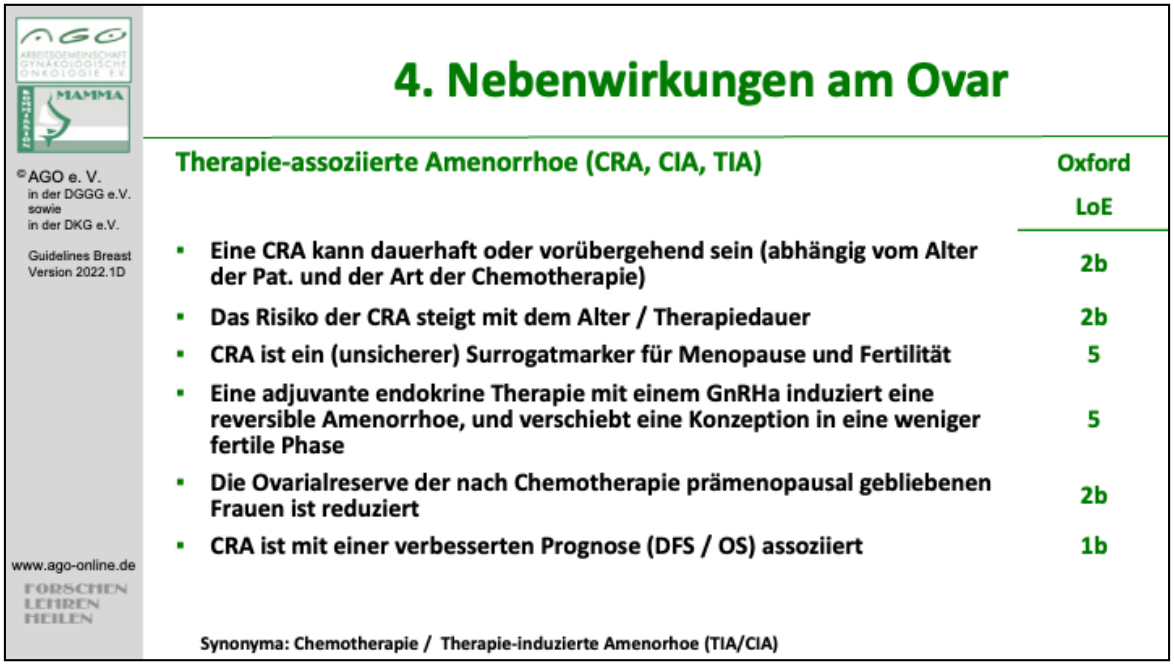

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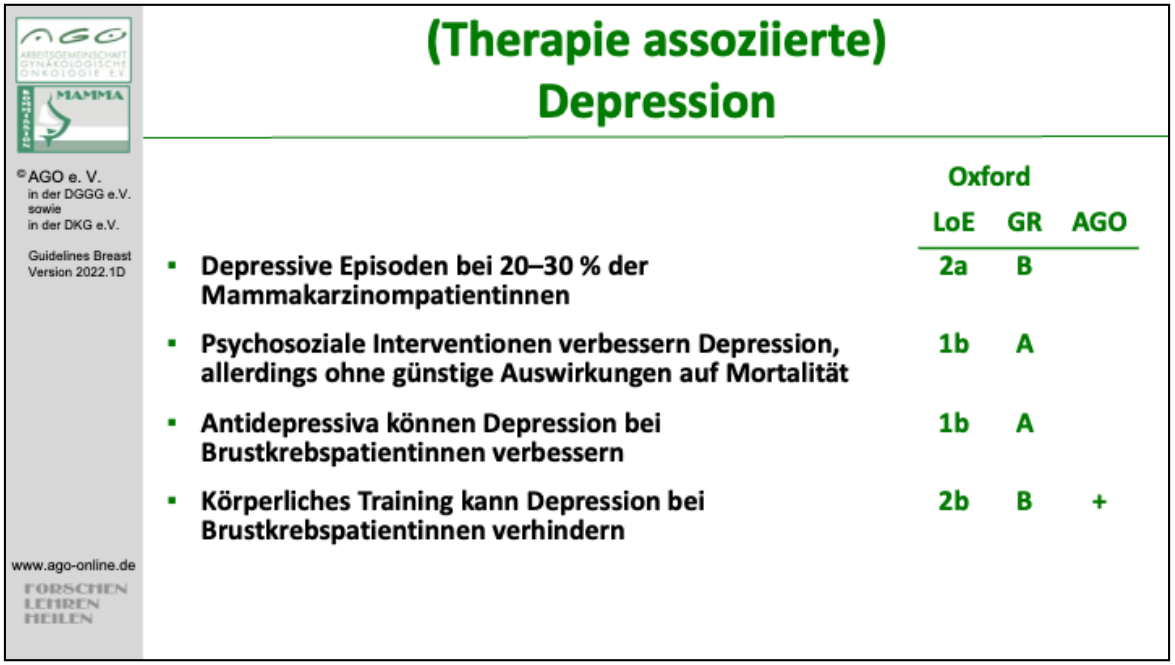
Nebenwirkungen nach Organsystemen
Inzidenz, Prävention, Therapie

5. Psychiatrische Erkrankungen

- Depression
- Fatigue
- Kognitive Störungen
- Schlafstörungen



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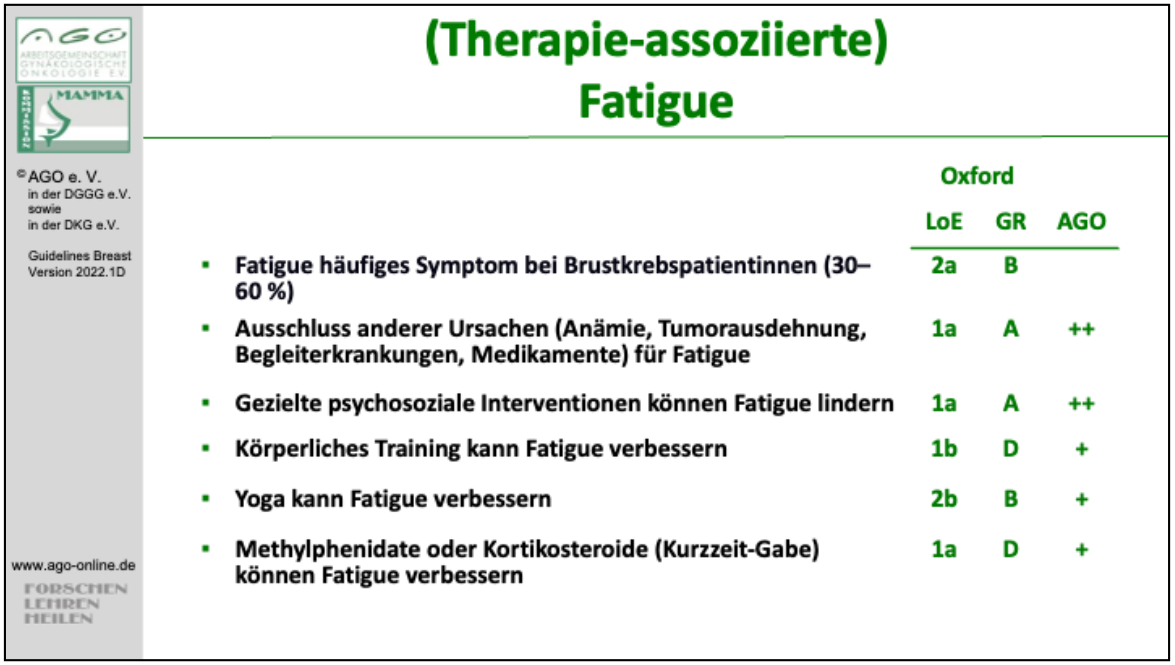

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Fatigue is frequently present…

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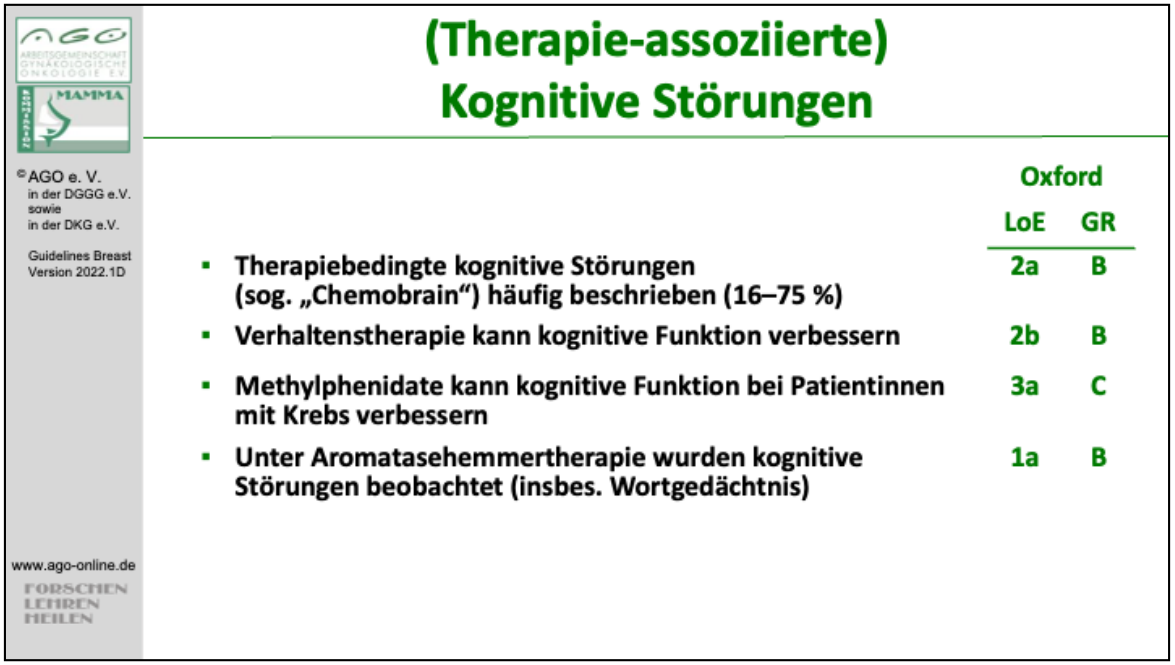

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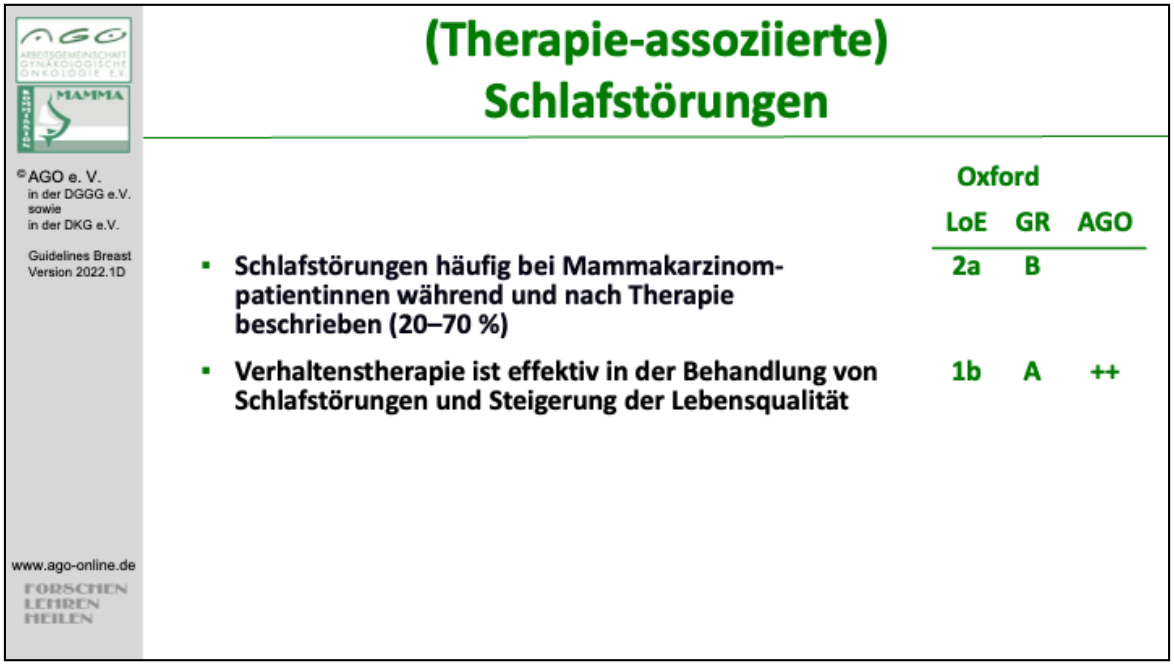

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Nebenwirkungen nach Organsystemen
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Guidelines Breast
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6. Erkrankungen des Nervensystems

- **Chemotherapie induzierte periphere Neuropathie (CIPN)**

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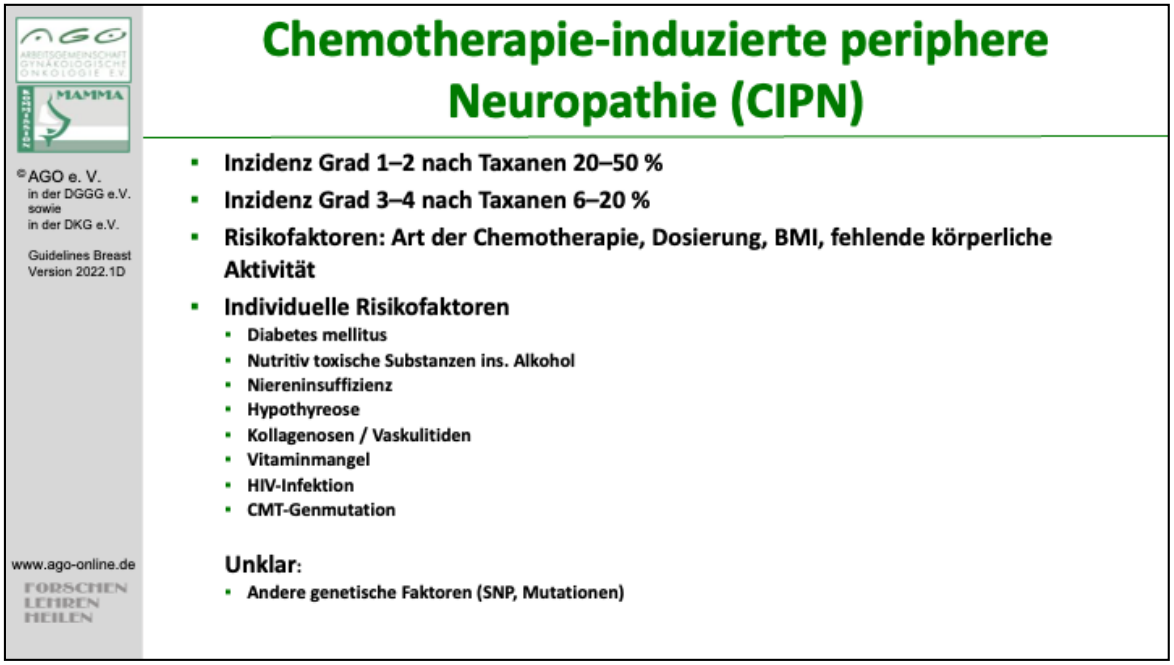

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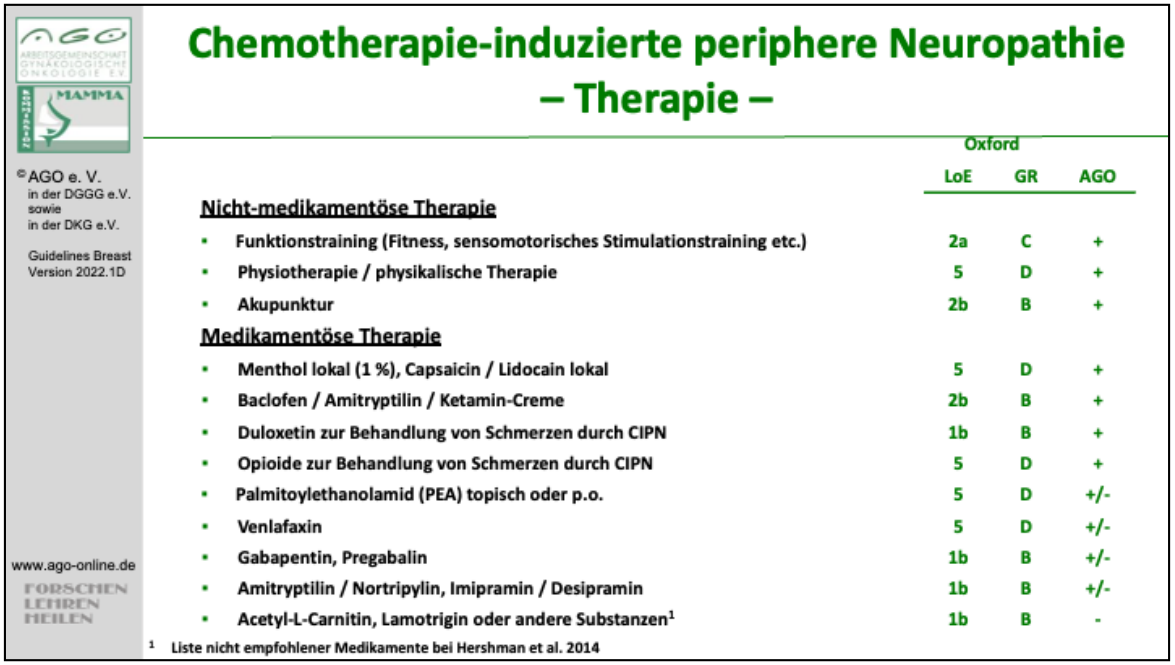

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7. Herzerkrankungen

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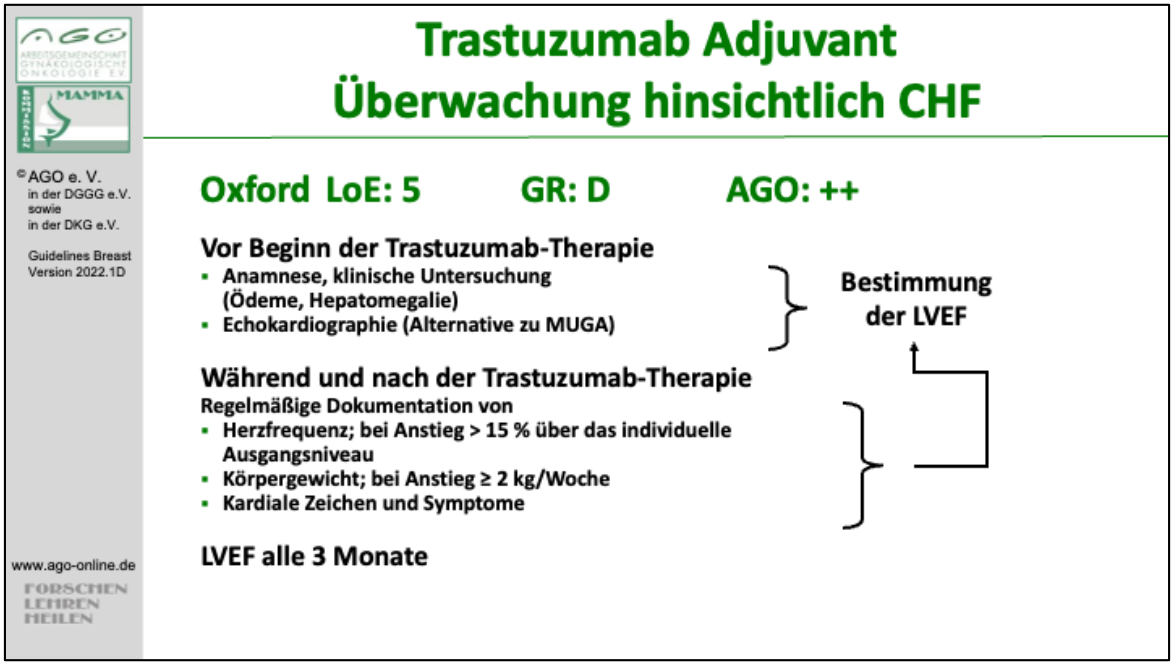

Statement: Cardiac Monitoring (5 D ++)

Vote result of the AGO recommendation: 100%

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Toxizitätssteigerungen durch Behandlungskombinationen

	Oxford LoE	Oxford GR	AGO
Kardiale Toxizität			
▪ Trastuzumab simultan zur Radiotherapie	2b	B	+
▪ Trastuzumab simultan zu Epirubicin	2b	B	+/-
▪ Trastuzumab simultan zu Doxorubicin	2b	B	-
▪ Anthrazykline simultan zur Radiotherapie	2c	C	-
Risiko Lungen- / Brustparenchymfibrosen			
▪ Tamoxifen simultan zu Radiotherapie	3	C	+/-
▪ Chemotherapie simultan zu Radiotherapie	1b	B	-

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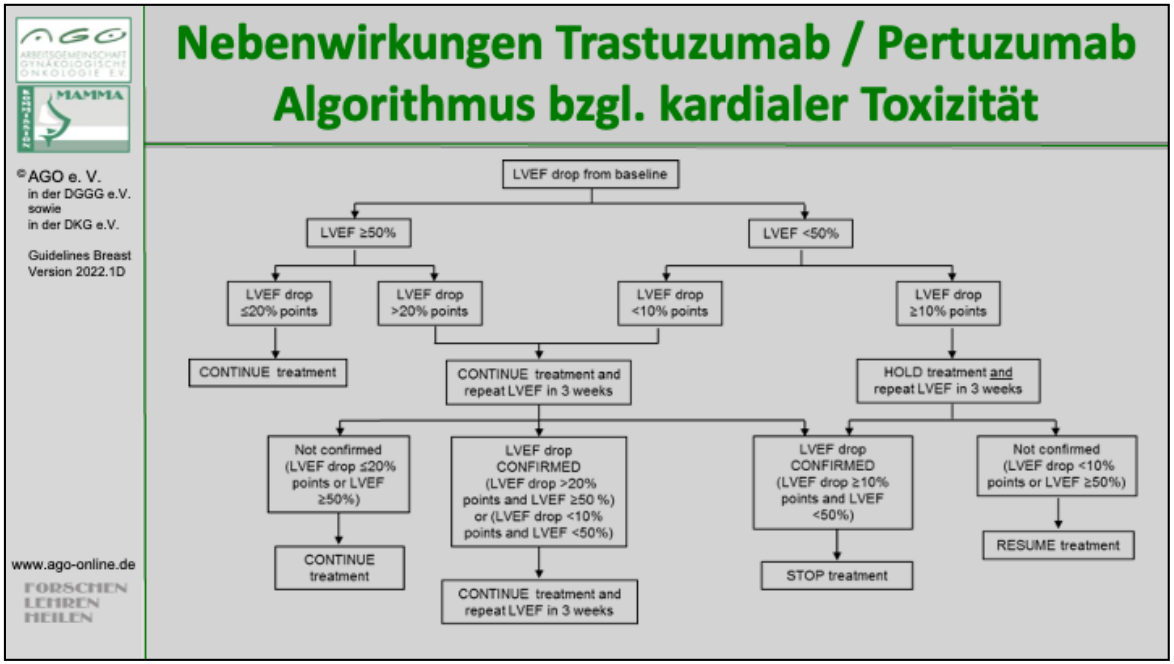

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   - Mukositis
     - Stomatitis (Everolimus)
   - Diarrhoe
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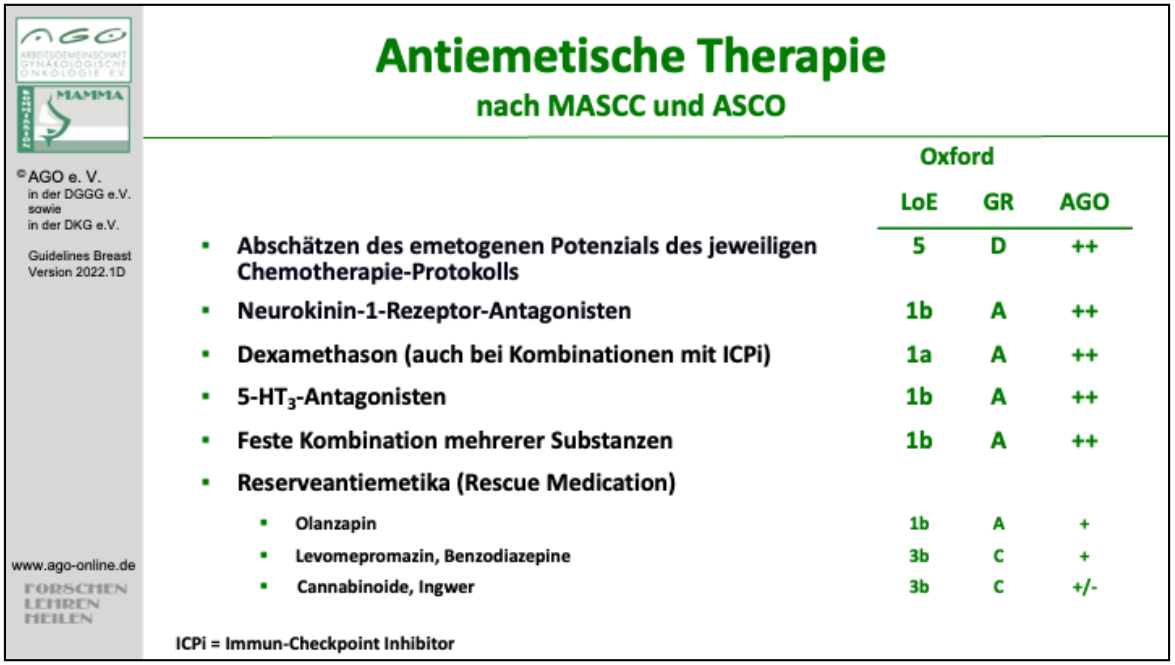

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Olanzapine

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Antiemetische Therapie
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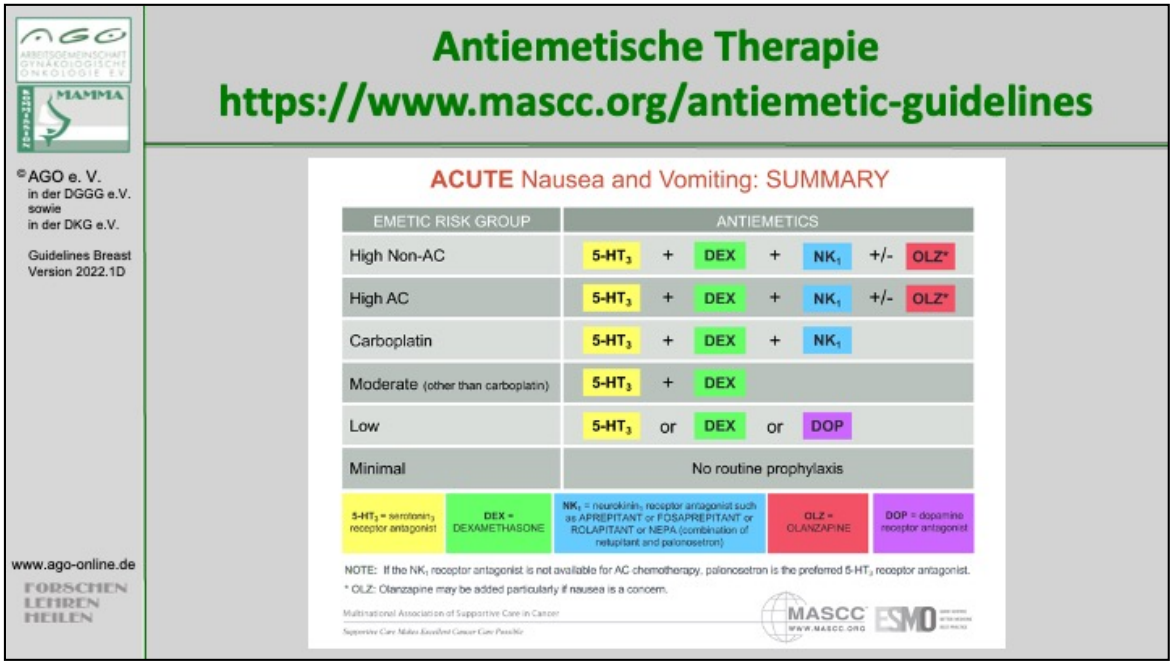

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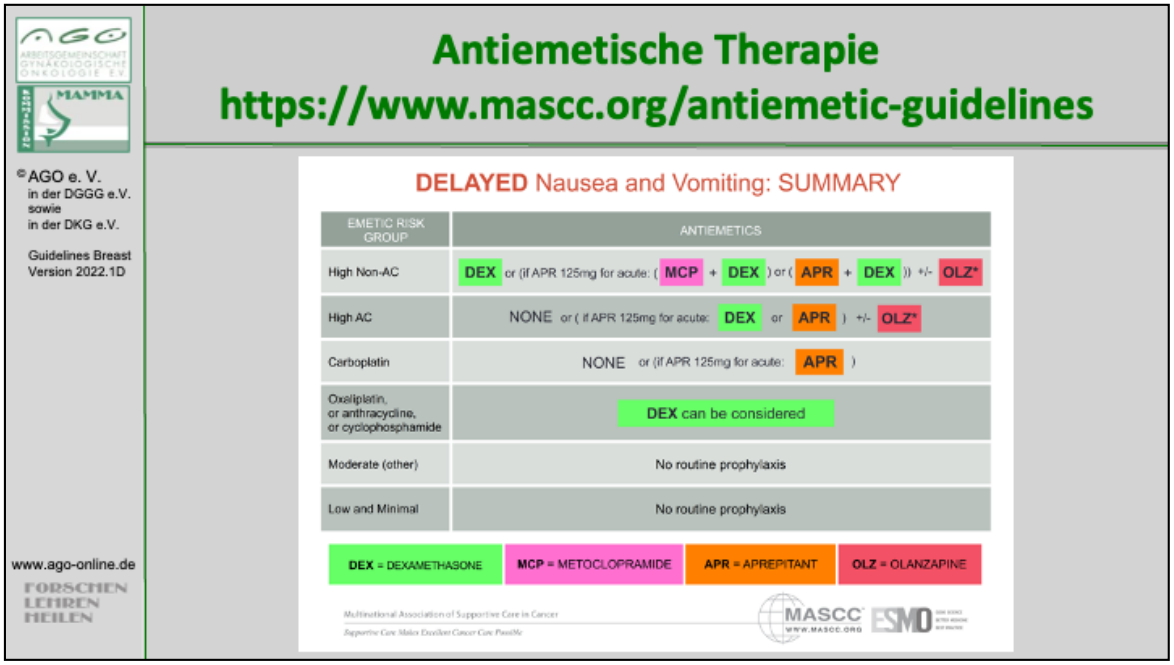

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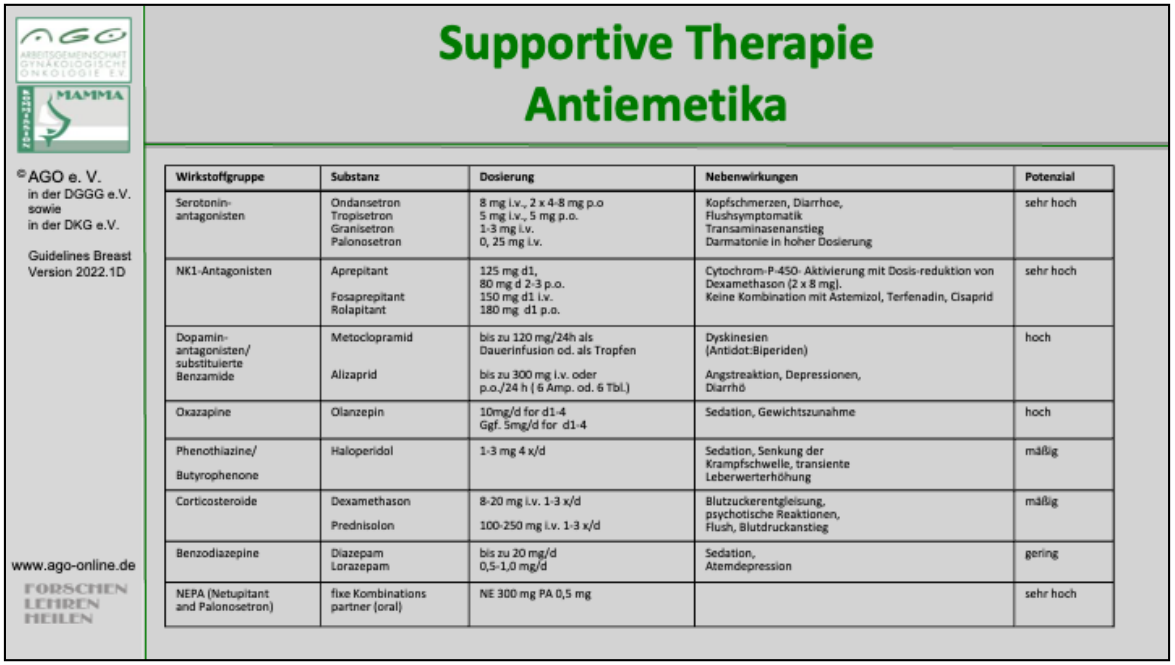

Supportive Therapie
Antiemetika

Wirkstoffgruppe	Substanz	Dosierung	Nebenwirkungen	Potenzial
Serotonin-antagonisten	Ondansetron Tropisetron Granisetron Palonosetron	8 mg i.v., 2 x 4-8 mg p.o 5 mg i.v., 5 mg p.o. 1-3 mg i.v. 0, 25 mg i.v.	Kopfschmerzen, Diarrhoe, Flushsymptomatik Transaminasenanstieg Darmatonie in hoher Dosierung	sehr hoch
NK1-Antagonisten	Aprepitant Fosaprepitant Rolapitant	125 mg d1, 80 mg d 2-3 p.o. 150 mg d1 i.v. 180 mg d1 p.o.	Cytochrom-P-450- Aktivierung mit Dosis-reduktion von Dexamethason (2 x 8 mg). Keine Kombination mit Astemizol, Terfenadin, Cisaprid	sehr hoch
Dopamin-antagonisten/ substituierte Benzamide	Metoclopramid Alizaprid	bis zu 120 mg/24h als Dauerinfusion od. als Tropfen bis zu 300 mg i.v. oder p.o./24 h (6 Amp. od. 6 Tbl.)	Dyskinesien (Antidot:Biperiden) Angstreaktion, Depressionen, Diarrhö	hoch
Oxazapine	Olanzepin	10mg/d for d1-4 Ggf. 5mg/d for d1-4	Sedation, Gewichtszunahme	hoch
Phenothiazine/ Butyrophenone	Haloperidol	1-3 mg 4 x/d	Sedation, Senkung der Krampfschwelle, transiente Leberwerterhöhung	mäßig
Corticosteroide	Dexamethason Prednisolon	8-20 mg i.v. 1-3 x/d 100-250 mg i.v. 1-3 x/d	Blutzuckerentgleisung, psychotische Reaktionen, Flush, Blutdruckanstieg	mäßig
Benzodiazepine	Diazepam Lorazepam	bis zu 20 mg/d 0,5-1,0 mg/d	Sedation, Atemdepression	gering
NEPA (Netupitant and Palonosetron)	fixe Kombinations partner (oral)	NE 300 mg PA 0,5 mg		sehr hoch

Olanzapine

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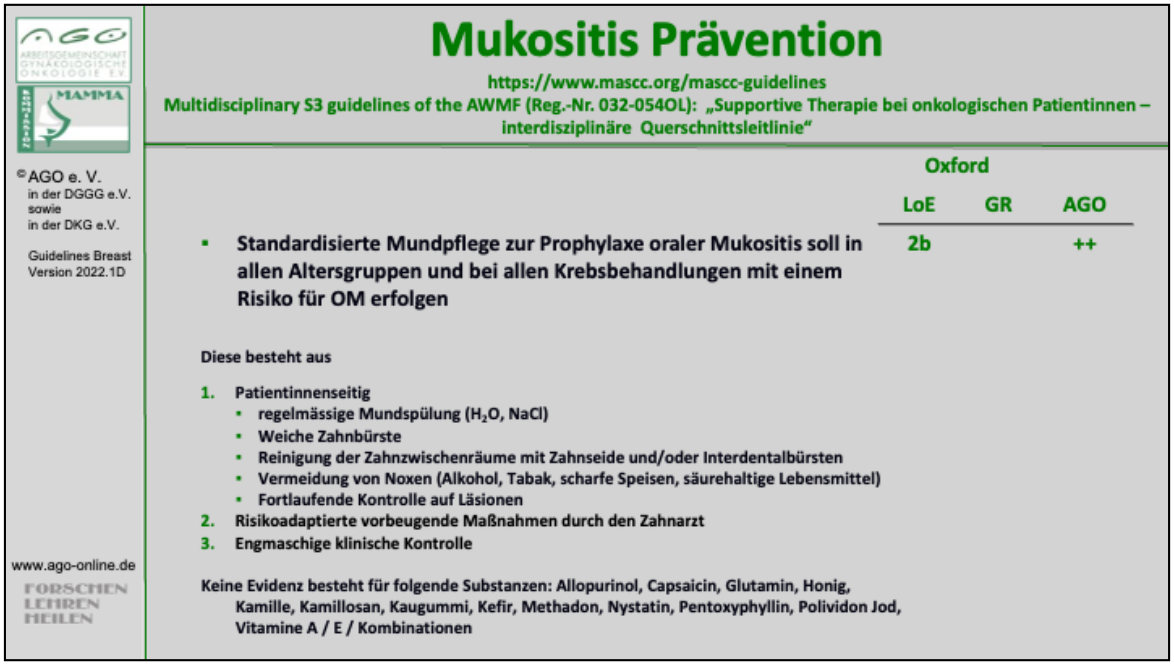

Relevant practice guideline

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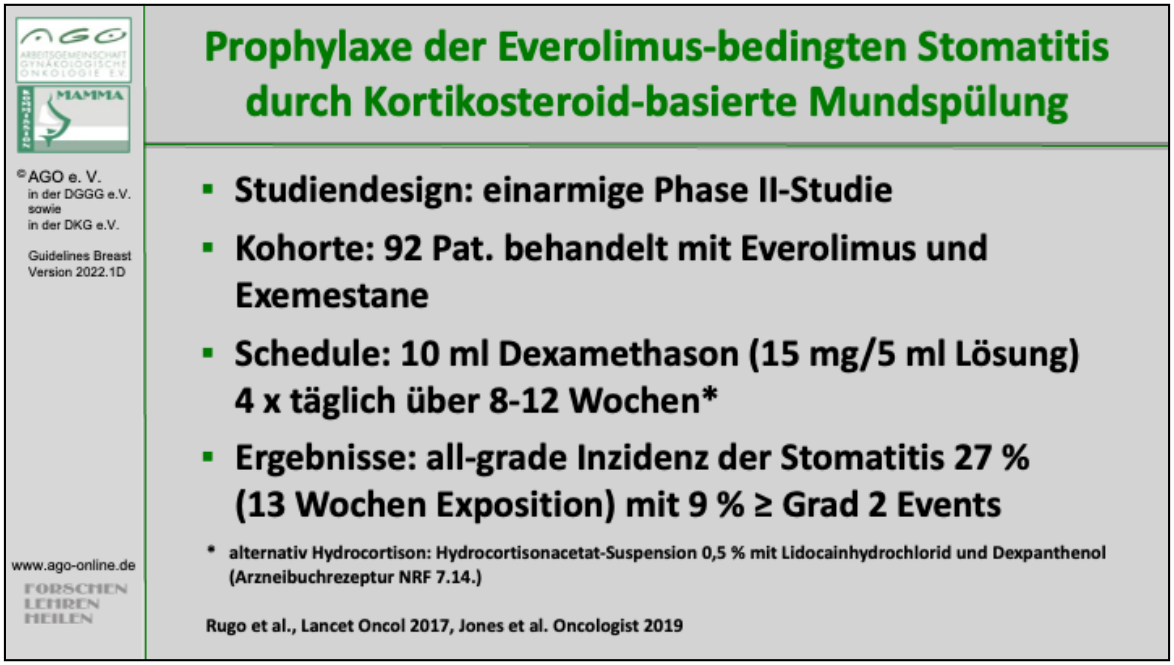

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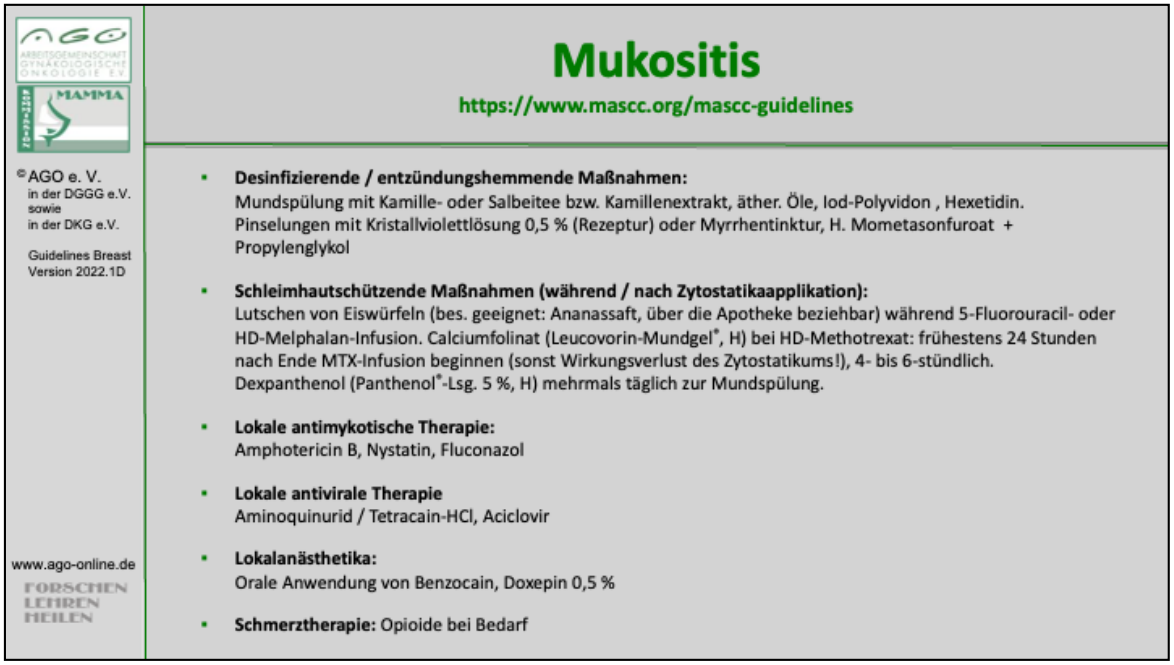

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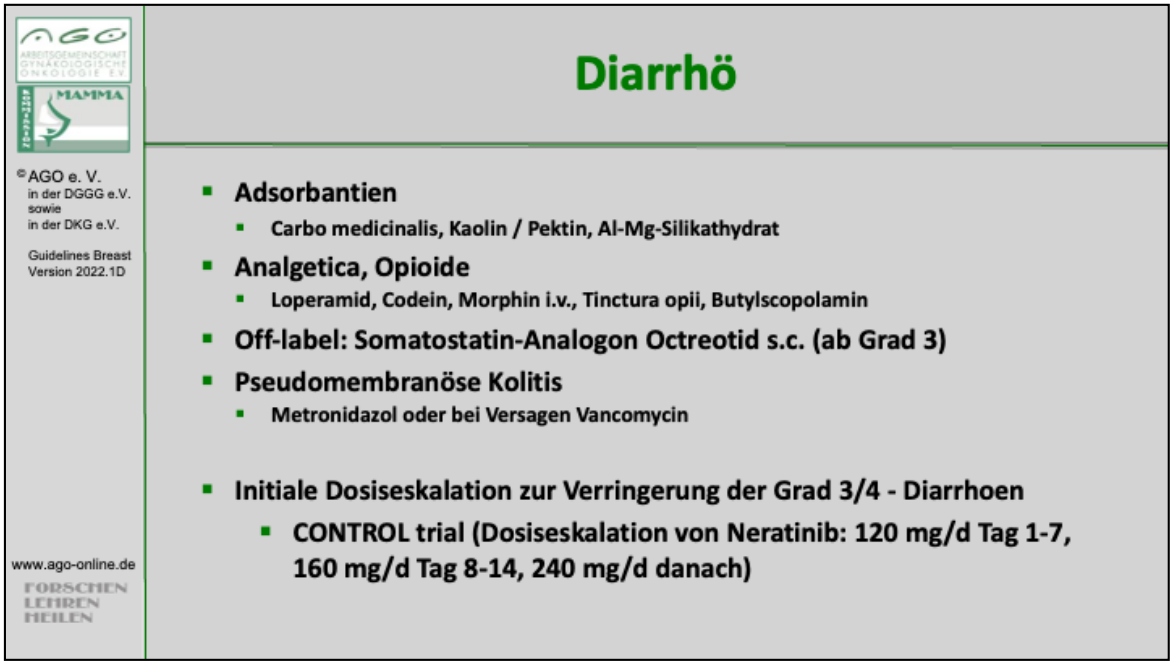

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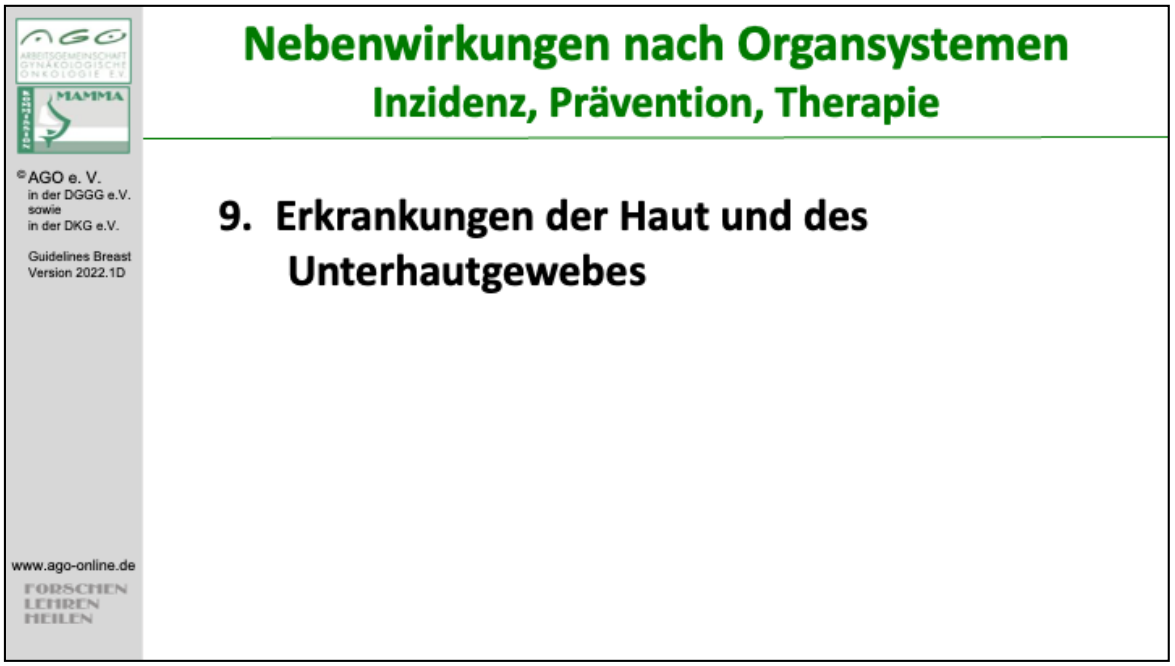

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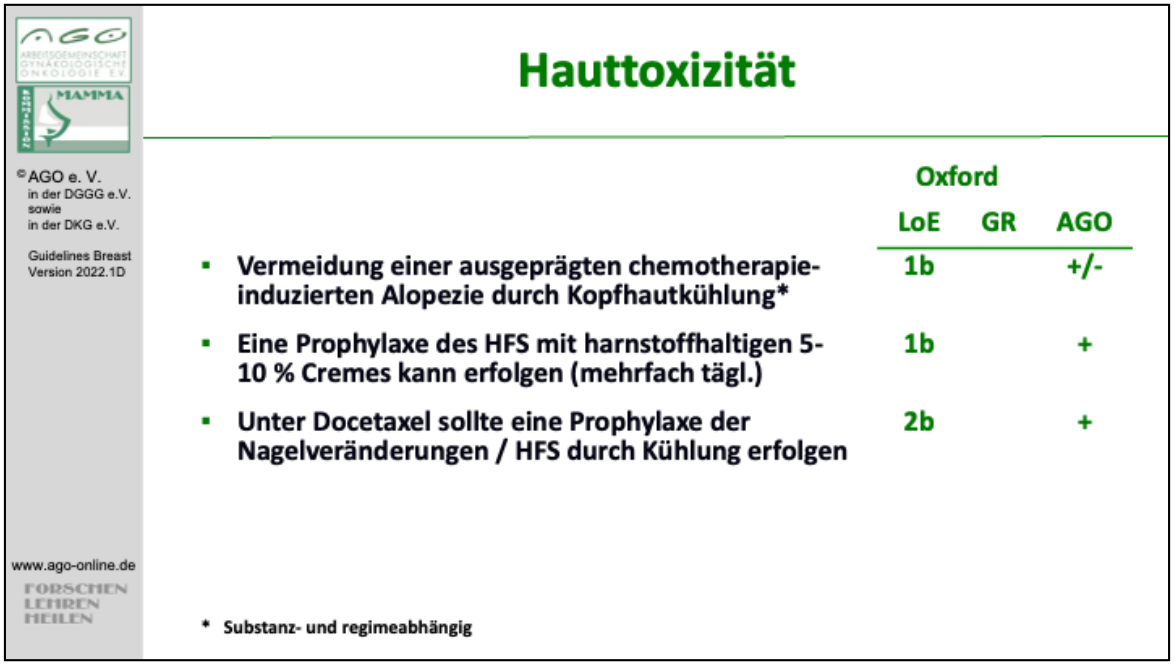

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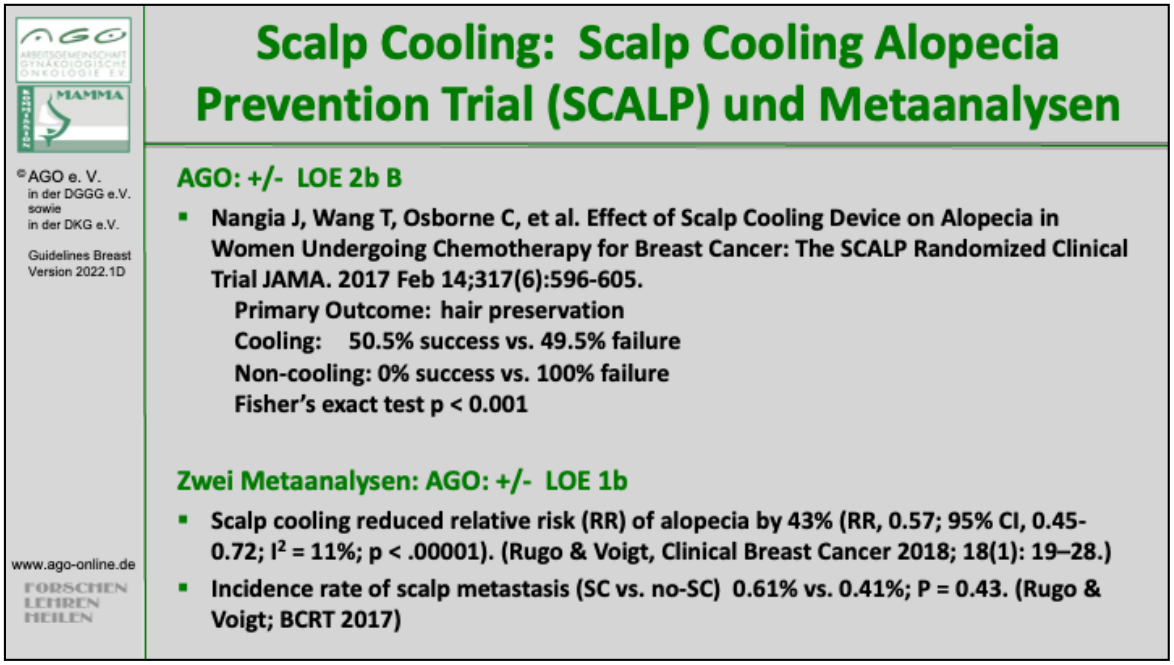

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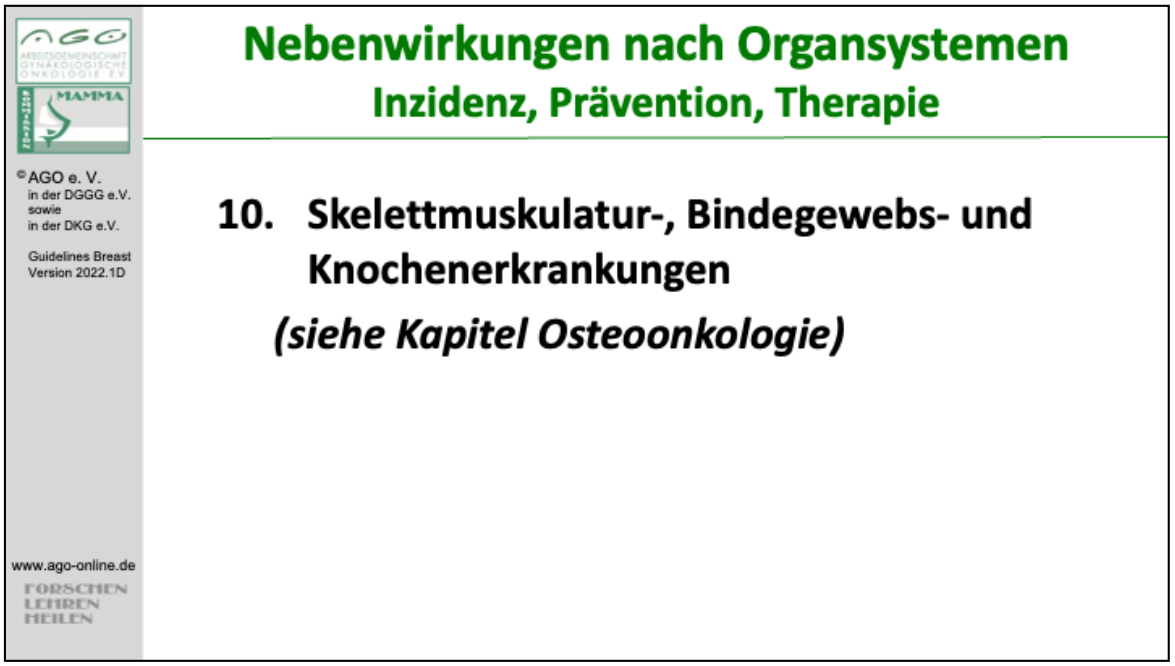

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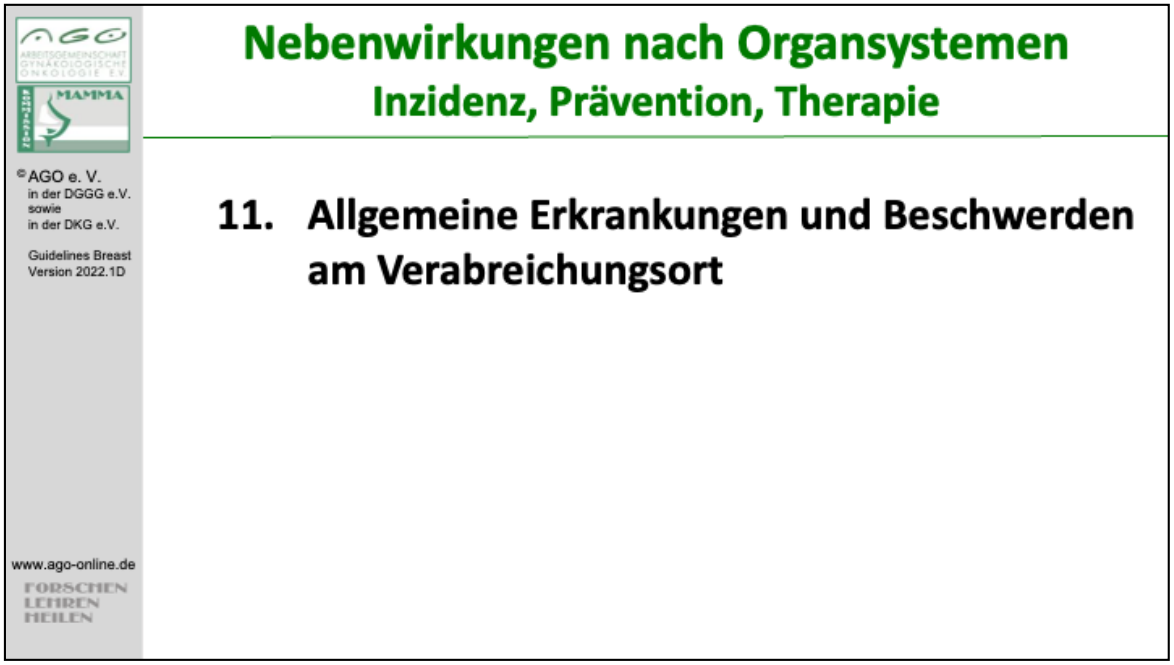

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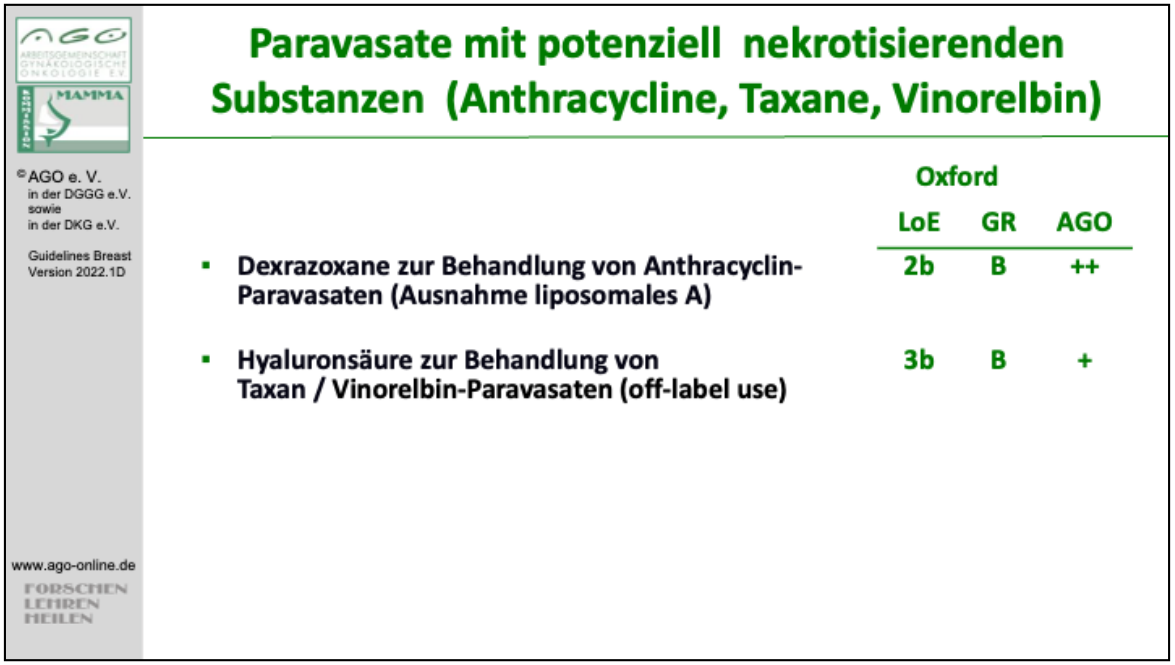

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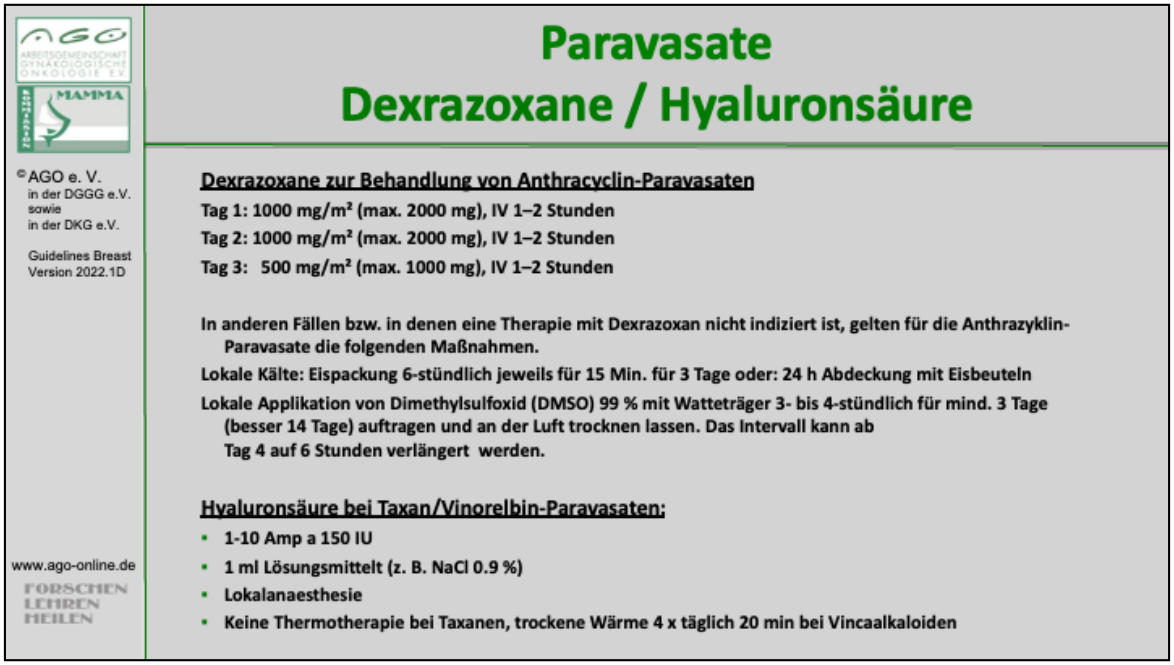
Hyaluronsäure

siehe S3-Leitlinie, Kapitel 11: Paravasate.



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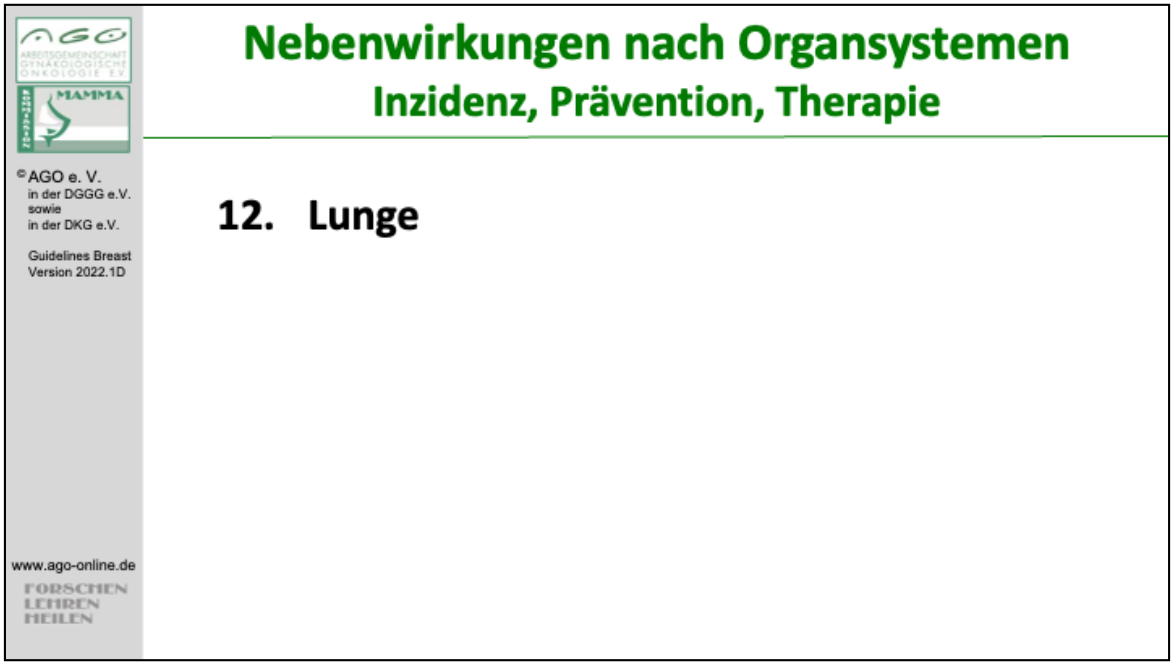

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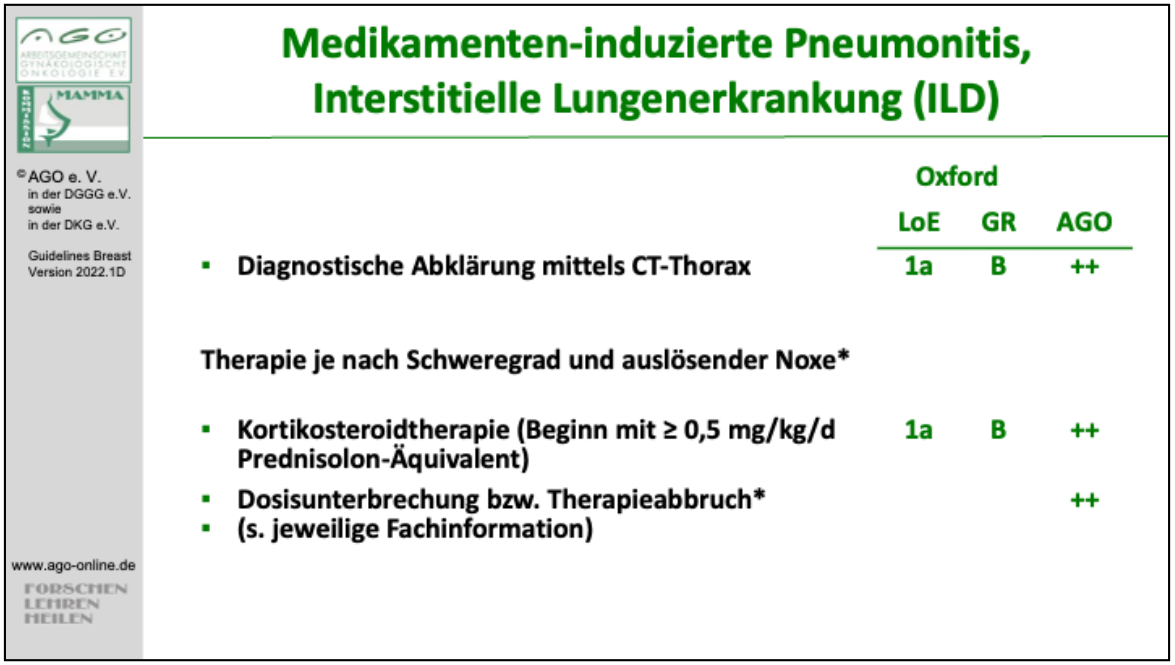

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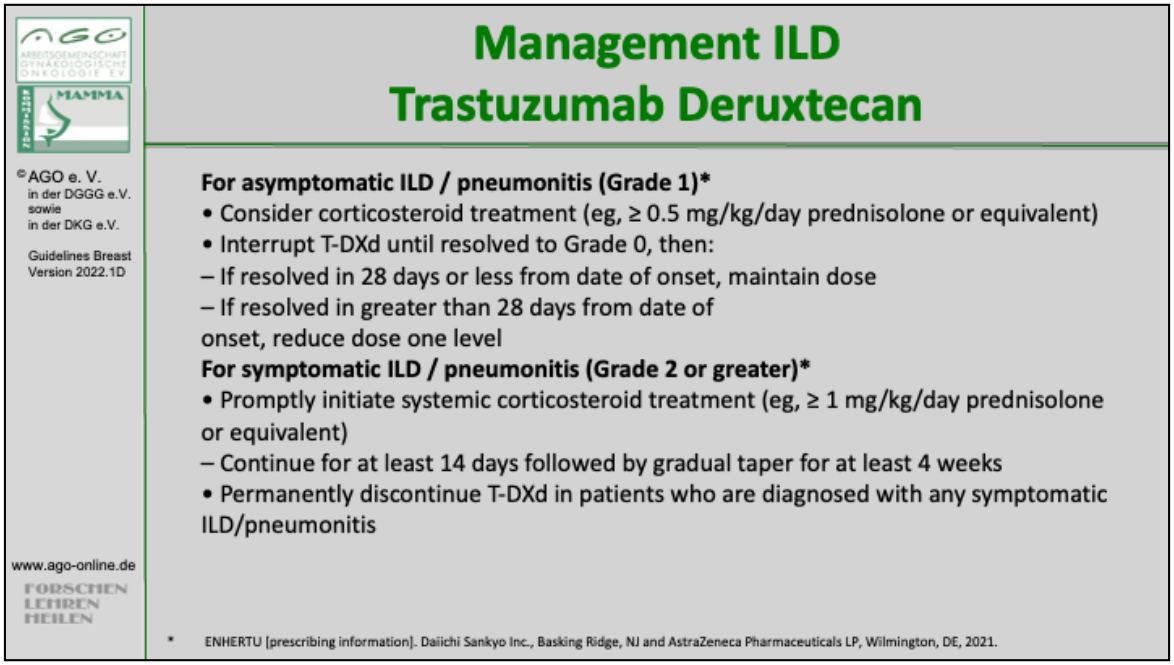

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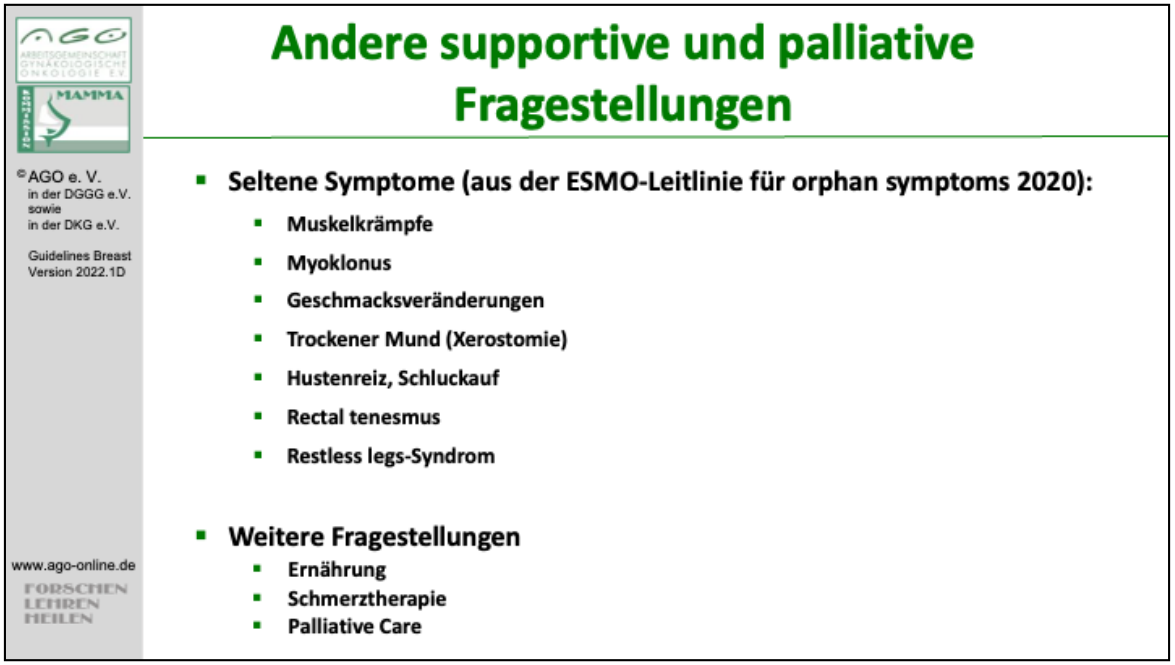

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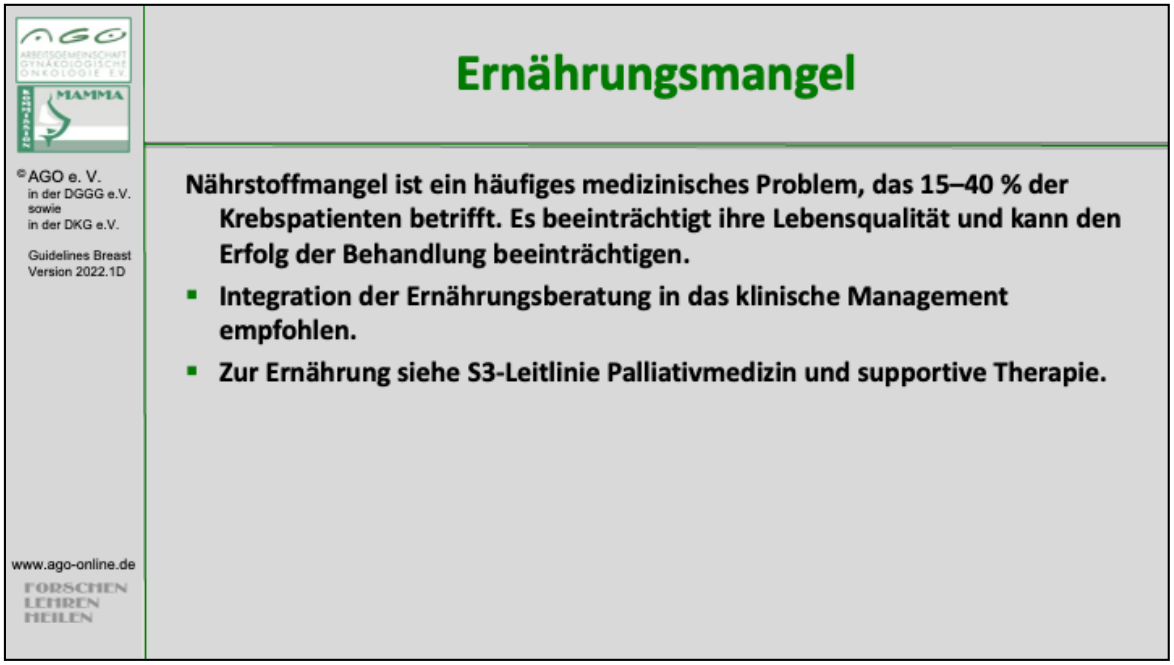

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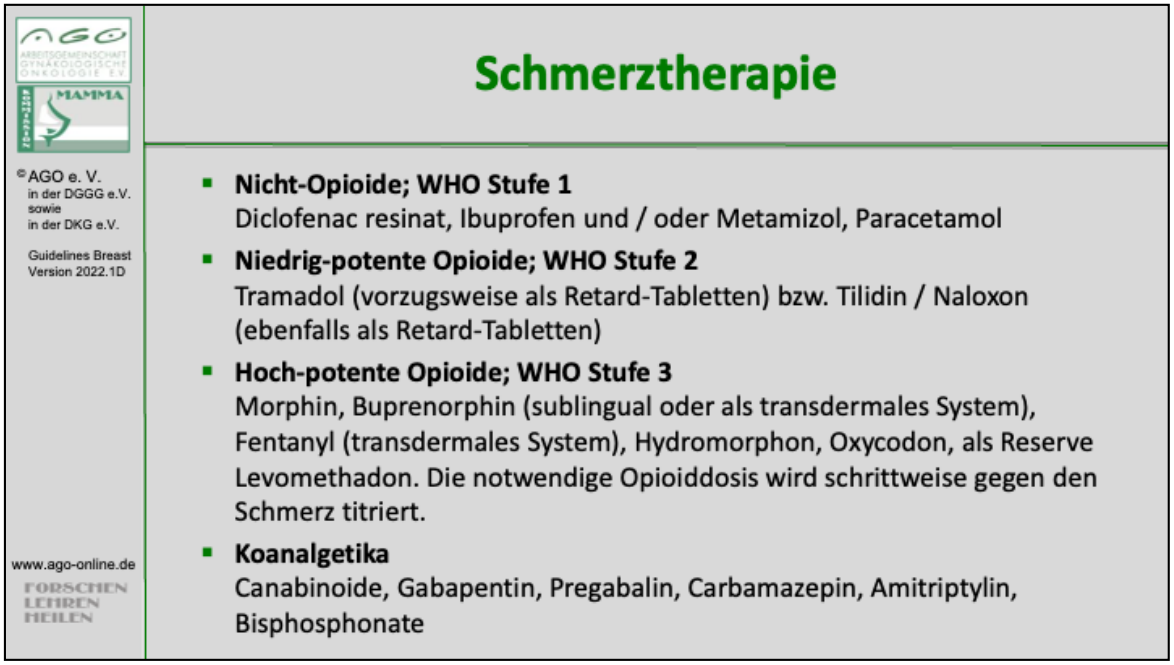

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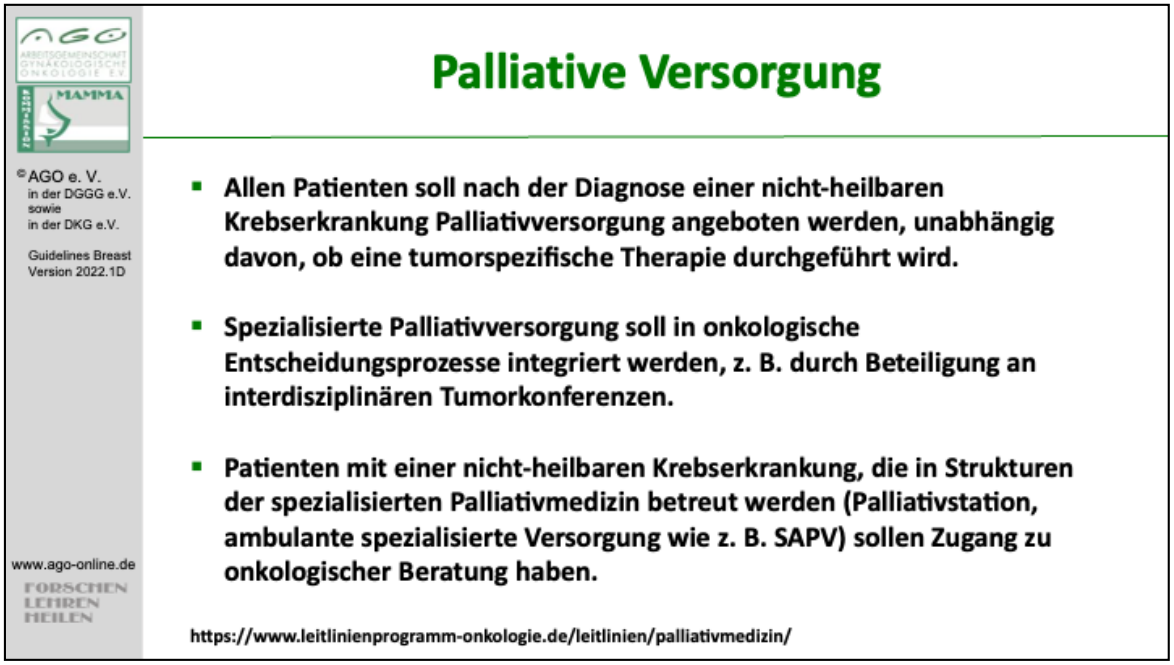

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