Screened data bases

Pubmed 2007 - 2022, ASCO 2010 – 2022, SABCS 2010 – 2021, Cochrane Data Base (2019)

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Supportive Care and Management of Side Effects

Guidelines Breast
Version 2022.1E

- **Versions 2002–2021:**
  Albert / Bauerfeind / Brunnert / Bischoff / Costa / Dall / Diel / Fersis / Friedrich / Friedrichs / Gerber / Göhring / Hanf / Harbeck / Heinrich / Huober / Jackisch / Lisboa / Lück / Lüftner / von Minckwitz / Möbus / Müller / Mundhenke / Nitz / Oberhoff / Rody / Schaller / Scharl / Schmidt / Schneeweiss / Schütz / Solomayer / Souchon / Stickeler / Thomssen / Untch

- **Version 2022:**
  Harbeck / Reimer

Guidelines - Evidence

Guidelines Breast
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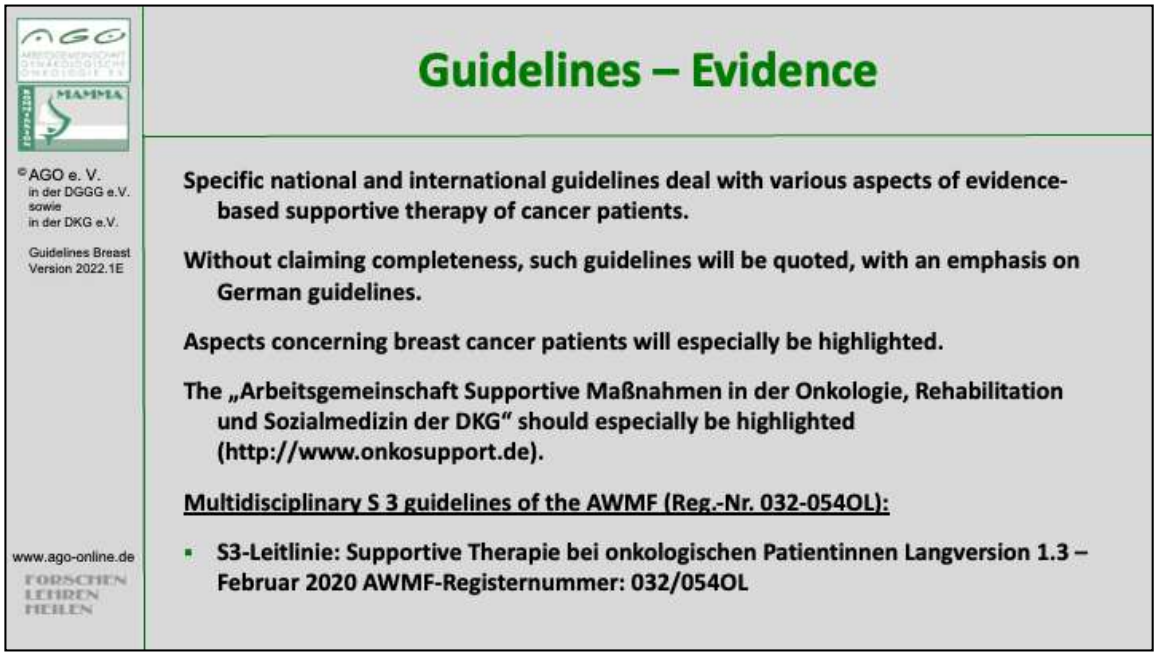

1. S3-Leitlinie Supportive Therapie:
   Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3 – Februar 2020 AWMF-Registernummer: 032/054OL Zugriff 25.12.2021 https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Supportivtherapie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

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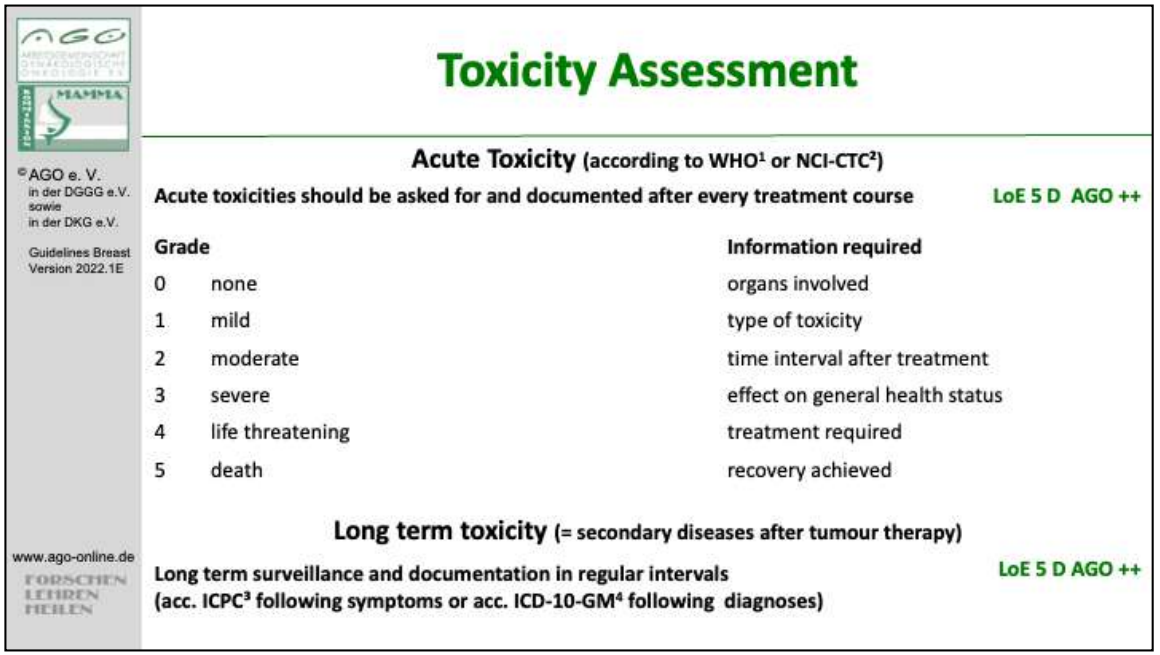
Toxicity Assessment

- Acute toxicity (NCI-CTCAE)
- Long term toxicity (ICPC, ICD-GM)



Acute Toxicity

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Acute Toxicity – Assessment after each cycle of therapy

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Long-term toxicity

1. International Classification of Primary Care (ICPC) revised December 2016, http://www.who.int/classifications/icd/adaptations/icpc2/en/ (Download 18.01.2018) or http://www.globalfamilydoctor.com/groups/WorkingParties/wicc.aspx (Download 18.01.2018)
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3. Kenyon M, Mayer DK, Owens AK. Late and long-term effects of breast cancer treatment and surveillance management for the

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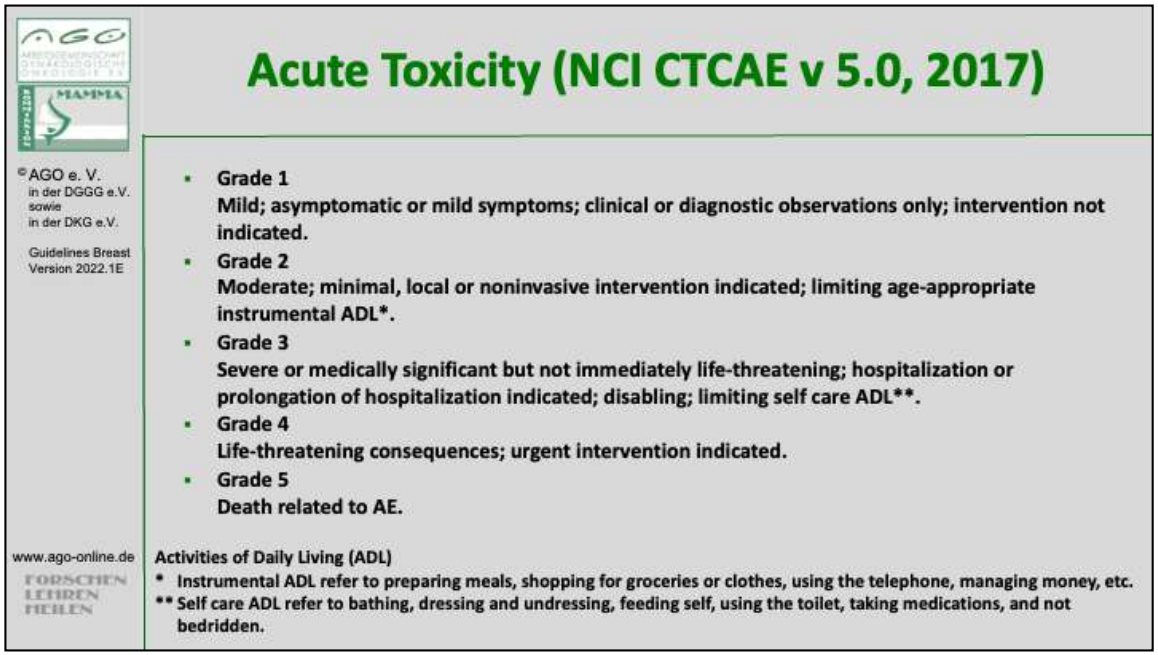
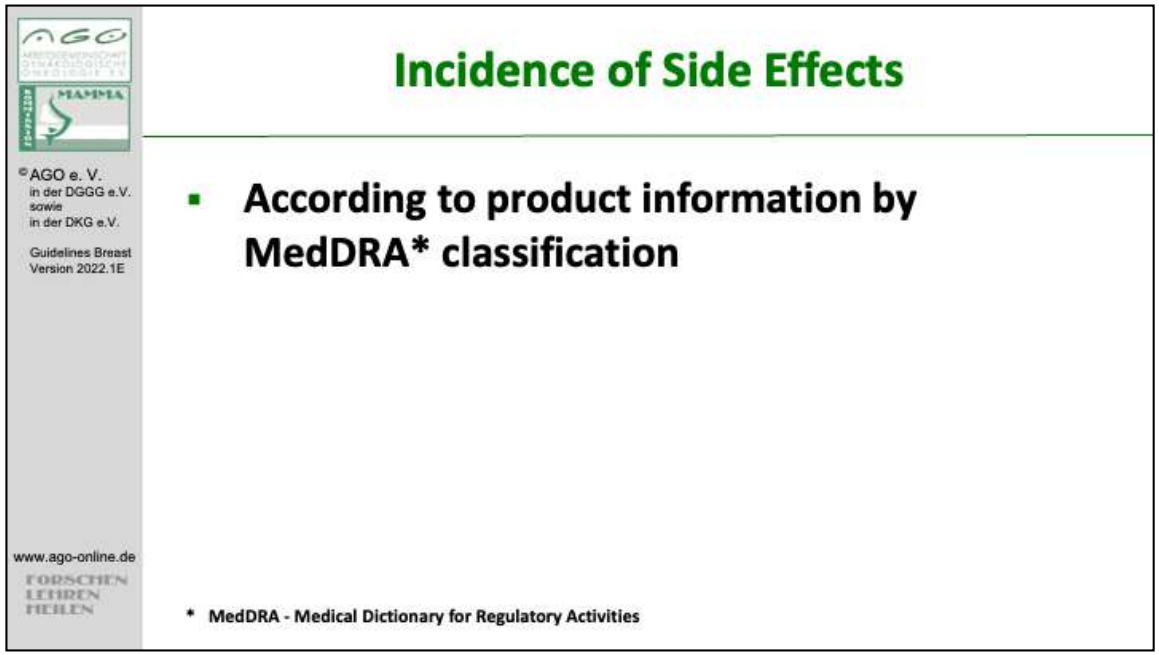
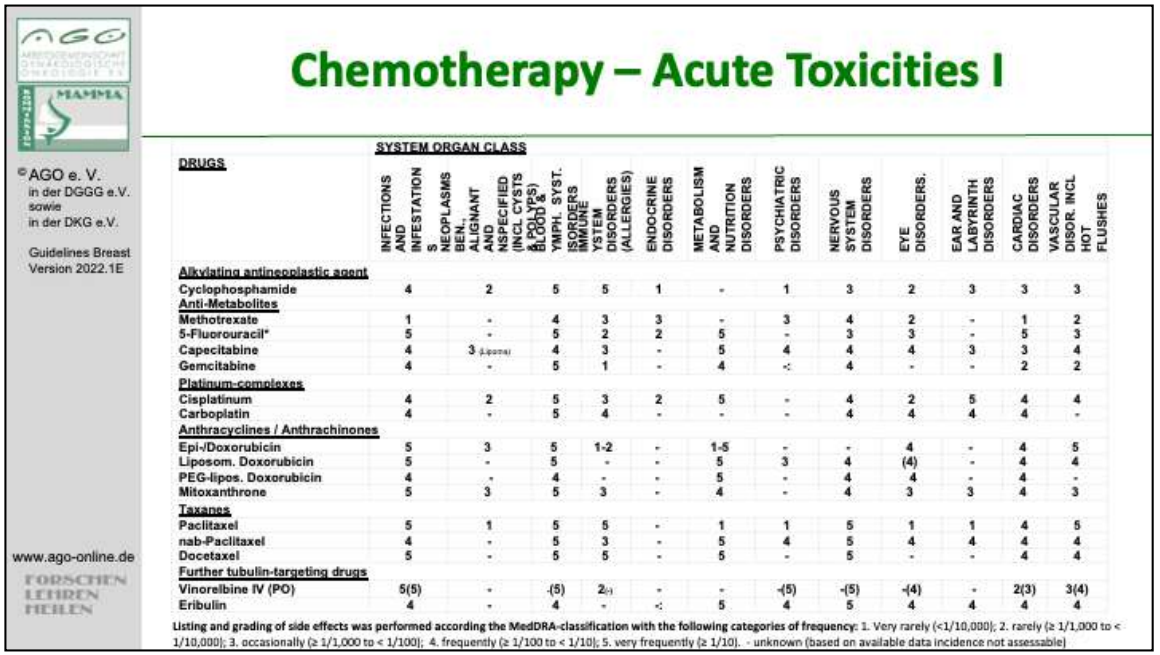


1. NCI, Bethesda, USA, Common Terminology Criteria for Adverse Events v5.0 (CTCAE; published 2017); https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50 (Download 18.01.2018)



*MedDRA - Medical Dictionary for Regulatory Activities

https://www.meddra.org/



Chemotherapy – Acute Toxicities I

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Guidelines Breast
Version 2022.1E

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DRUGS	SYSTEM ORGAN CLASS: INFECTIONS AND INFESTATIONS	NEOPLASMS BEN., ALIGNANT AND NSPECIFIED (INCL CYSTS & POLYPS)	BLOOD & YMPH. SYST.	ISORDERS IMMUNE YSTEM DISORDERS (ALLERGIES)	ENDOCRINE DISORDERS	METABOLISM AND NUTRITION DISORDERS	PSYCHIATRIC DISORDERS	NERVOUS SYSTEM DISORDERS	EYE DISORDERS.	EAR AND LABYRINTH DISORDERS	CARDIAC DISORDERS	VASCULAR DISOR. INCL HOT FLUSHES
Alkylating antineoplastic agent												
Cyclophosphamide	4	2	5	5	1	-	1	3	2	3	3	3
Anti-Metabolites												
Methotrexate	1	-	4	3	3	-	3	4	2	-	1	2
5-Fluorouracil*	5	-	5	2	2	5	-	3	3	-	5	3
Capecitabine	4	3 (Lipoma)	4	3	-	5	4	4	4	3	3	4
Gemcitabine	4	-	5	1	-	4	-:	4	-	-	2	2
Platinum-complexes												
Cisplatinum	4	2	5	3	2	5	-	4	2	5	4	4
Carboplatin	4	-	5	4	-	-	-	4	4	4	4	-
Anthracyclines / Anthrachinones												
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	-
Mitoxanthrone	5	3	5	3	-	4	-	4	3	3	4	3
Taxanes												
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
Further tubulin-targeting drugs												
Vinorelbine IV (PO)	5(5)	-	-(5)	2(-)	-	-	-(5)	-(5)	-(4)	-	2(3)	3(4)
Eribulin	4	-	4	-	-:	5	4	5	4	4	4	4

Listing and grading of side effects was performed according the MedDRA-classification with the following categories of frequency: 1. Very rarely (<1/10,000); 2. rarely (≥ 1/1,000 to < 1/10,000); 3. occasionally (≥ 1/1,000 to < 1/100); 4. frequently (≥ 1/100 to < 1/10); 5. very frequently (≥ 1/10). - unknown (based on available data incidence not assessable)

Side effect categories - 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

Sources for product information (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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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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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.
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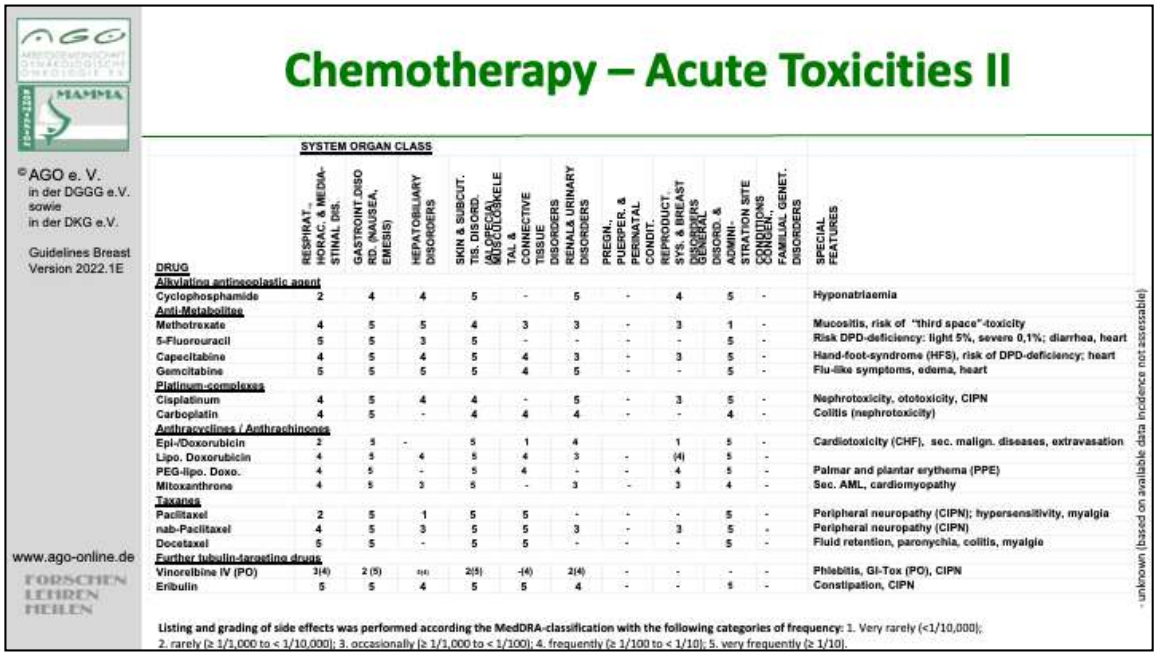
12. Madeddu C, Deidda M, Piras A, et al. Pathophysiology of cardiotoxicity induced by nonanthracycline chemotherapy. J Cardiovasc Med (Hagerstown). 2016 May;17 Suppl 1 Special issue on Cardiotoxicity from Antiblastic Drugs and Cardioprotection:e12-e18. Review.



Chemotherapy – Acute Toxicities II

Guidelines Breast
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	SYSTEM ORGAN CLASS										
DRUG	RESPIRAT., HORAC. & MEDIASTINAL DIS.	GASTROINT.DISORD. (NAUSEA, EMESIS)	HEPATOBILIARY DISORDERS	SKIN & SUBCUT. TIS. DISORD. (ALOPECIA)	MUSCOLOSKELETAL & CONNECTIVE TISSUE DISORDERS	RENAL& URINARY DISORDERS	PREGN., PUERPER.& PERINATAL CONDIT.	REPRODUCT SYS. & BREAST DISORDS	GENERAL DISORD. & ADMINISTRATION SITE CONDITIONS	CONGEN., FAMILIAL GENET. DISORDERS	SPECIAL FEATURES
Alkylating antineoplastic agent											
Cyclophosphamide	2	4	4	5	-	5	-	4	5	-	Hyponatriaemia
Anti-Metabolites											
Methotrexate	4	5	5	4	3	3	-	3	1	-	Mucositis, risk of "third space"-toxicity
5-Fluorouracil	5	5	3	5	-	-	-	-	5	-	Risk DPD-deficiency: light 5%, severe 0,1%; diarrhea, heart
Capecitabine	4	5	4	5	4	3	-	3	5	-	Hand-foot-syndrome (HFS), risk of DPD-deficiency; heart
Gemcitabine	5	5	5	5	4	5	-	-	5	-	Flu-like symptoms, edema, heart
Platinum-complexes											
Cisplatinum	4	5	4	4	-	5	-	3	5	-	Nephrotoxicity, ototoxicity, CIPN
Carboplatin	4	5	-	4	4	4	-	-	4	-	Colitis (nephrotoxicity)
Anthracyclines / Anthrachinones											
Epi-/Doxorubicin	2	5	-	5	1	4		1	5	-	Cardiotoxicity (CHF), sec. malign. diseases, extravasation
Lipo. Doxorubicin	4	5	4	5	4	3	-	(4)	5	-	
PEG-lipo. Doxo.	4	5	-	5	4	-	-	4	5	-	Palmar and plantar erythema (PPE)
Mitoxanthrone	4	5	3	5	-	3	-	3	4	-	Sec. AML, cardiomyopathy
Taxanes											
Paclitaxel	2	5	1	5	5	-	-	-	5	-	Peripheral neuropathy (CIPN); hypersensitivity, myalgia
nab-Paclitaxel	4	5	3	5	5	3	-	3	5	-	Peripheral neuropathy (CIPN)
Docetaxel	5	5	-	5	5	-	-	-	5	-	Fluid retention, paronychia, colitis, myalgia
Further tubulin-targeting drugs											
Vinorelbine IV (PO)	3(4)	2 (5)	1(4)	2(5)	-(4)	2(4)	-	-	-	-	Phlebitis, GI-Tox (PO), CIPN
Eribulin	5	5	4	5	5	4	-	-	5	-	Constipation, CIPN

- unknown (based on available data incidence not assessable)

Listing and grading of side effects was performed according the MedDRA-classification with the following categories of frequency: 1. Very rarely (<1/10,000); 2. rarely (≥ 1/1,000 to < 1/10,000); 3. occasionally (≥ 1/1,000 to < 1/100); 4. frequently (≥ 1/100 to < 1/10); 5. very frequently (≥ 1/10).

Abbreviations

AML = Acute myeloid Leucemia; DPD = Dihydropyrimidin-Dehydrogenase); CHF = congestive heart failure; CIPN = Chemotherapy-induced peripheral neuropathy; HFS = Hand-Foot-Syndrom; PPE = Palmar and plantar Erythema

Side effect categories - 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

Sources for product information (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
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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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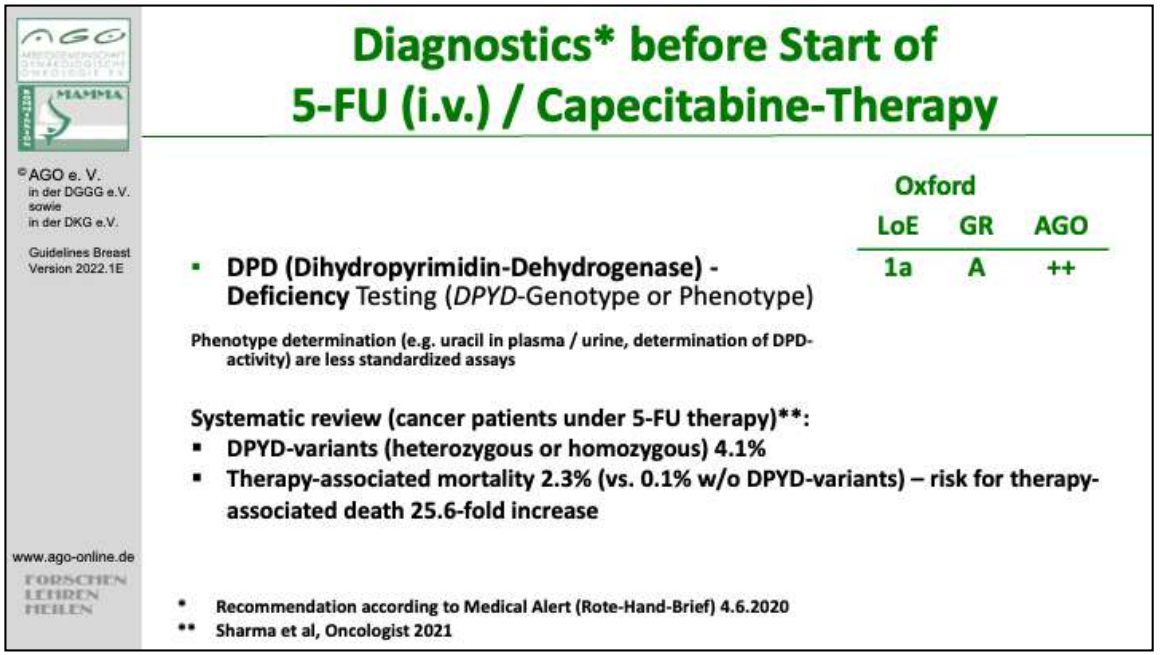
12. Madeddu C, Deidda M, Piras A, et al. Pathophysiology of cardiotoxicity induced by nonanthracycline chemotherapy. J Cardiovasc Med (Hagerstown). 2016 May;17 Suppl 1 Special issue on Cardiotoxicity from Antiblastic Drugs and Cardioprotection:e12-e18. Review.



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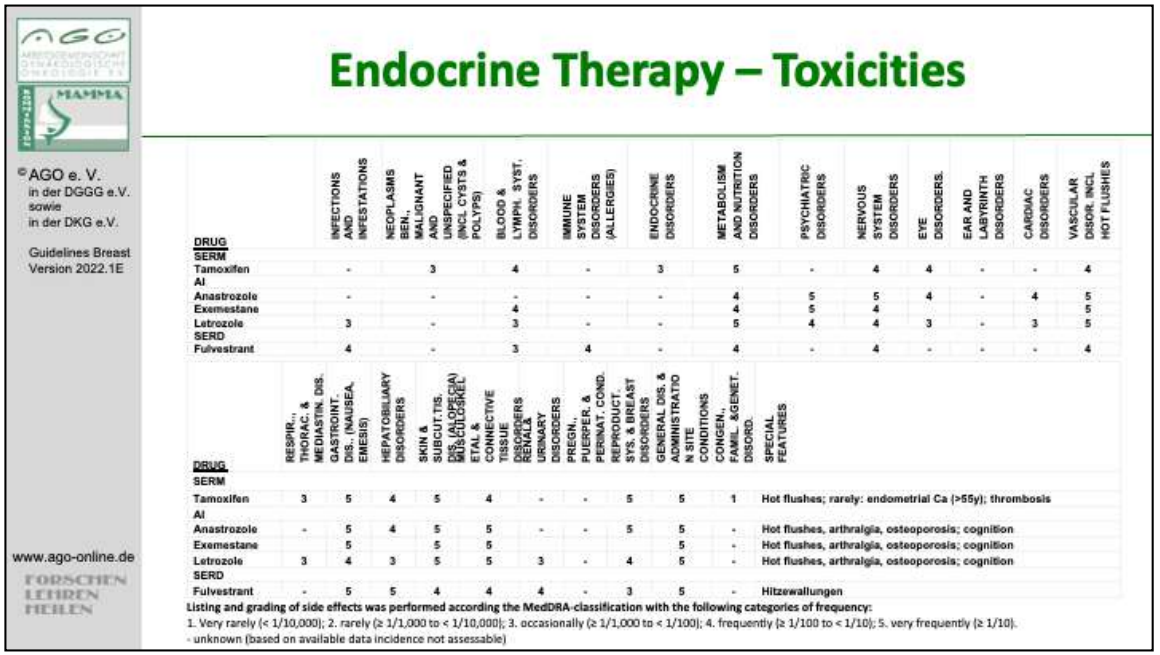

Endocrine Therapy – Toxicities

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Guidelines Breast
Version 2022.1E

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DRUG	INFECTIONS AND INFESTATIONS	NEOPLASMS BEN., MALIGNANT AND UNSPECIFIED (INCL CYSTS & POLYPS)	BLOOD & LYMPH. SYST. DISORDERS	IMMUNE SYSTEM DISORDERS (ALLERGIES)	ENDOCRINE DISORDERS	METABOLISM AND NUTRITION DISORDERS	PSYCHIATRIC DISORDERS	NERVOUS SYSTEM DISORDERS	EYE DISORDERS	EAR AND LABYRINTH DISORDERS	CARDIAC DISORDERS	VASCULAR DISOR. INCL. HOT FLUSHES
SERM												
Tamoxifen	-	3	4	-	3	5	-	4	4	-	-	4
AI												
Anastrozole	-	-	-	-	-	4	5	5	4	-	4	5
Exemestane			4			4	5	4				5
Letrozole	3	-	3	-	-	5	4	4	3	-	3	5
SERD												
Fulvestrant	4	-	3	4	-	4	-	4	-	-	-	4

DRUG	RESPIR., THORAC. & MEDIASTIN. DIS.	GASTROINT. DIS., (NAUSEA, EMESIS)	HEPATOBILIARY DISORDERS	SKIN & SUBCUT.TIS. DIS. (ALOPECIA) MUSCULOSKEL ETAL & CONNECTIVE TISSUE DISORDERS	RENAL & URINARY DISORDERS	PREGN., PUERPER. & PERINAT. COND.	REPRODUCT. SYS. & BREAST DISORDERS	GENERAL DIS. & ADMINISTRATIO N SITE CONDITIONS	CONGEN., FAMIL. &GENET. DISORD.	SPECIAL FEATURES
SERM										
Tamoxifen	3	5	4	5	4	-	-	5	5	1	Hot flushes; rarely: endometrial Ca (>55y); thrombosis
AI										
Anastrozole	-	5	4	5	5	-	-	5	5	-	Hot flushes, arthralgia, osteoporosis; cognition
Exemestane		5		5	5				5	-	Hot flushes, arthralgia, osteoporosis; cognition
Letrozole	3	4	3	5	5	3	-	4	5	-	Hot flushes, arthralgia, osteoporosis; cognition
SERD										
Fulvestrant	-	5	5	4	4	4	-	3	5	-	Hitzewallungen

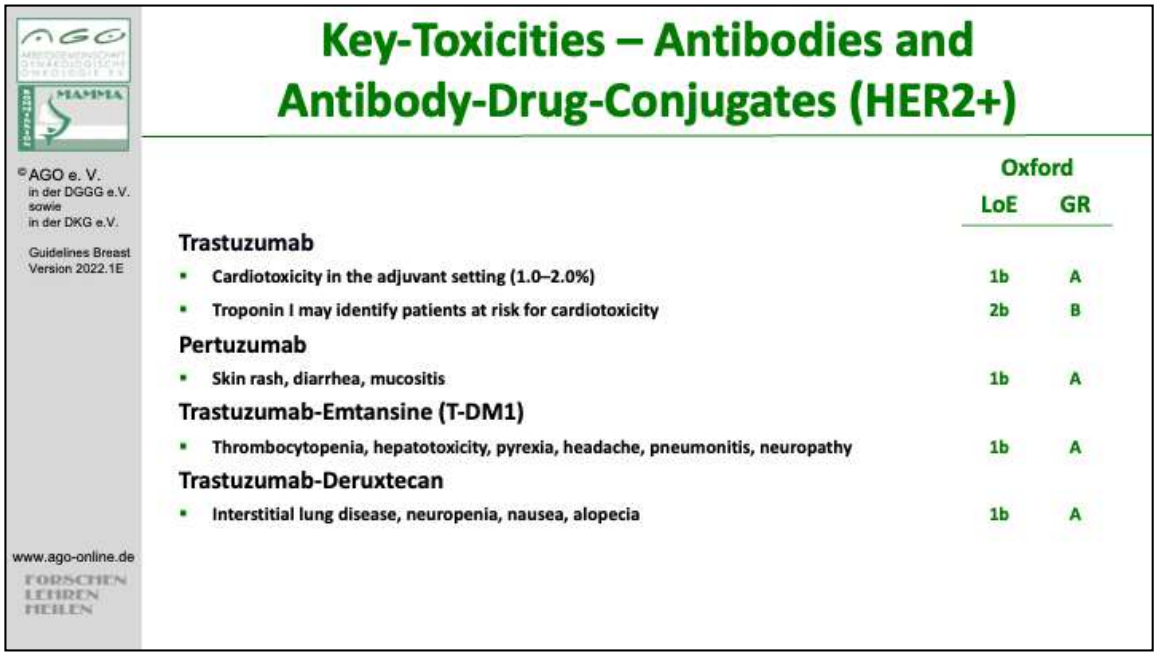
Listing and grading of side effects was performed according the MedDRA-classification with the following categories of frequency:
1. Very rarely (< 1/10,000); 2. rarely (≥ 1/1,000 to < 1/10,000); 3. occasionally (≥ 1/1,000 to < 1/100); 4. frequently (≥ 1/100 to < 1/10); 5. very frequently (≥ 1/10).
- unknown (based on available data incidence not assessable)

<u>Side effect categories- 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>Sources for product information (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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Troponin I

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T-DM1

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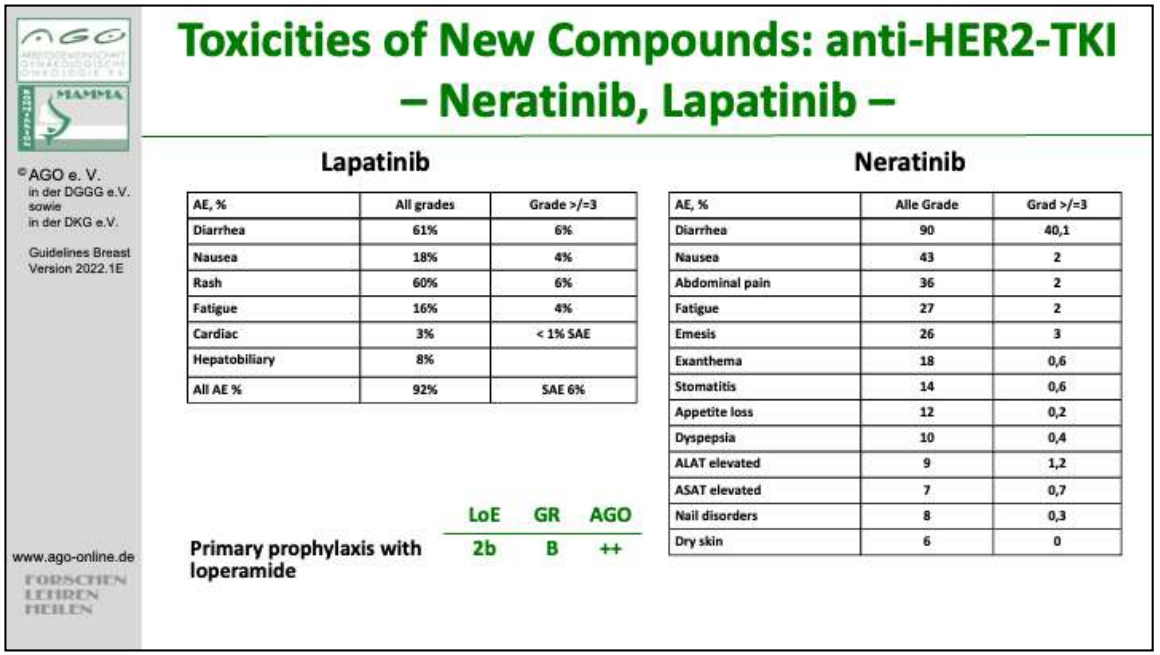

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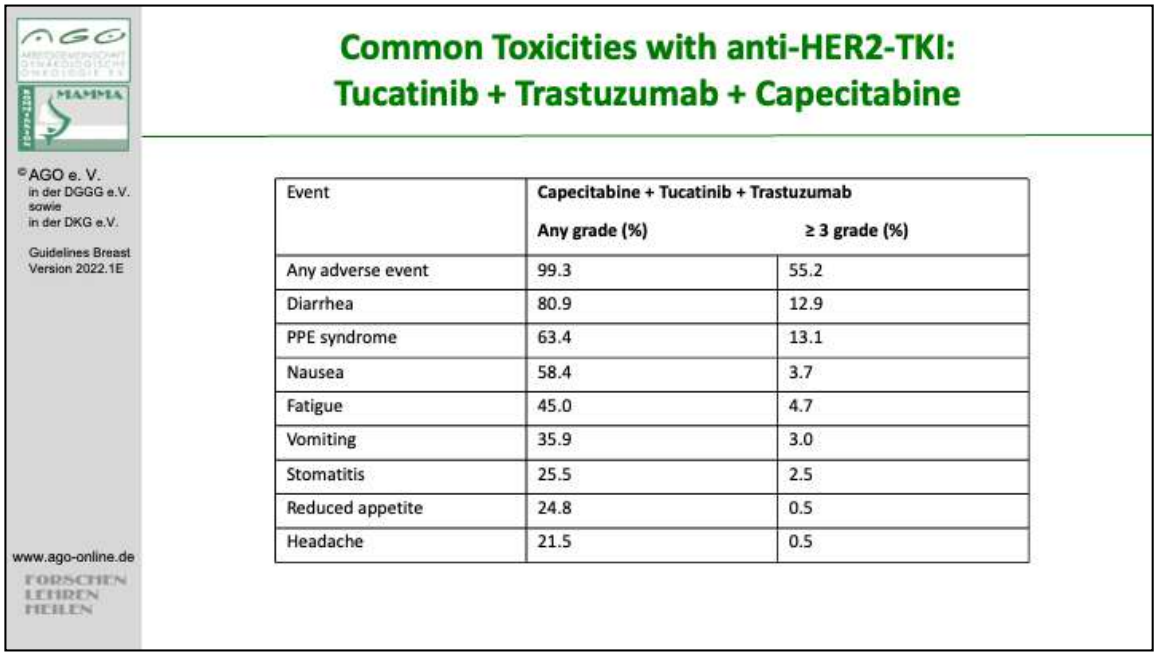

Common Toxicities with anti-HER2-TKI: Tucatinib + Trastuzumab + Capecitabine

Event	Capecitabine + Tucatinib + Trastuzumab	
	Any grade (%)	≥ 3 grade (%)
Any adverse event	99.3	55.2
Diarrhea	80.9	12.9
PPE syndrome	63.4	13.1
Nausea	58.4	3.7
Fatigue	45.0	4.7
Vomiting	35.9	3.0
Stomatitis	25.5	2.5
Reduced appetite	24.8	0.5
Headache	21.5	0.5

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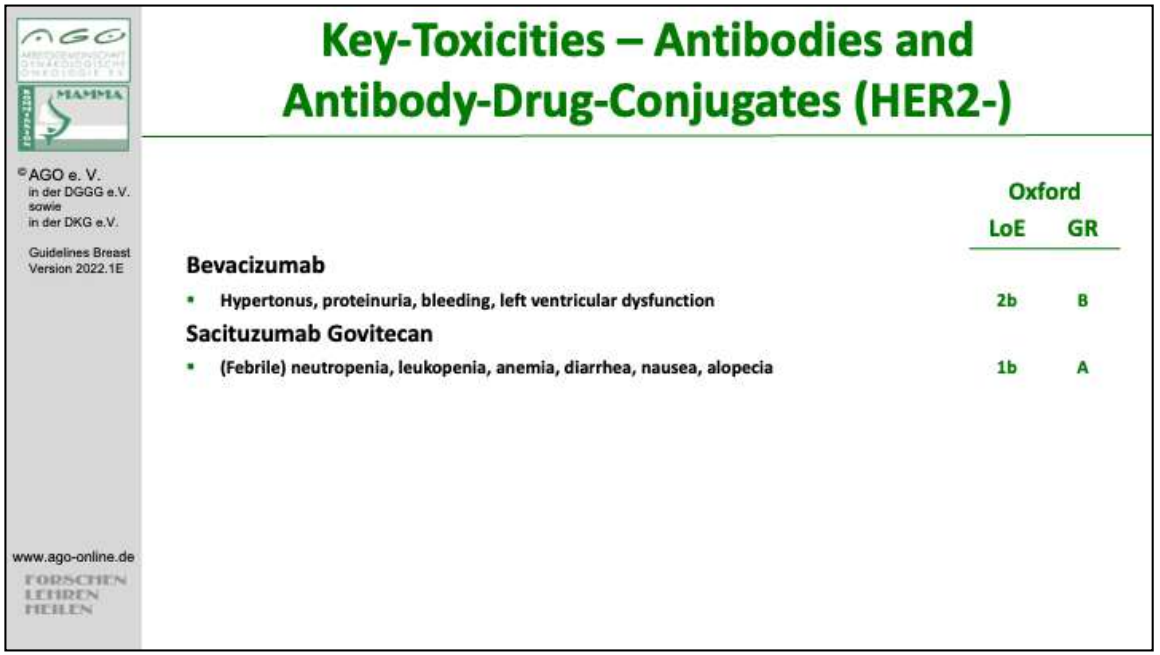

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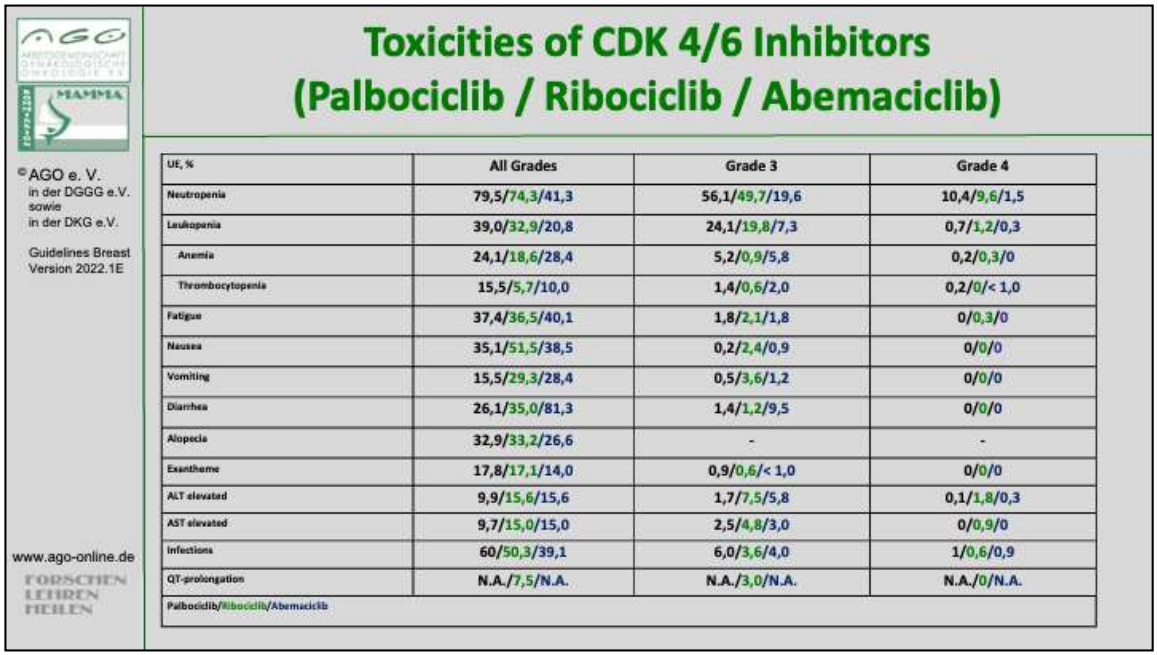

UE, %	All Grades	Grade 3	Grade 4
Neutropenia	79,5/74,3/41,3	56,1/49,7/19,6	10,4/9,6/1,5
Leukopenia	39,0/32,9/20,8	24,1/19,8/7,3	0,7/1,2/0,3
Anemia	24,1/18,6/28,4	5,2/0,9/5,8	0,2/0,3/0
Thrombocytopenia	15,5/5,7/10,0	1,4/0,6/2,0	0,2/0/< 1,0
Fatigue	37,4/36,5/40,1	1,8/2,1/1,8	0/0,3/0
Nausea	35,1/51,5/38,5	0,2/2,4/0,9	0/0/0
Vomiting	15,5/29,3/28,4	0,5/3,6/1,2	0/0/0
Diarrhea	26,1/35,0/81,3	1,4/1,2/9,5	0/0/0
Alopecia	32,9/33,2/26,6	-	-
Exantheme	17,8/17,1/14,0	0,9/0,6/< 1,0	0/0/0
ALT elevated	9,9/15,6/15,6	1,7/7,5/5,8	0,1/1,8/0,3
AST elevated	9,7/15,0/15,0	2,5/4,8/3,0	0/0,9/0
Infections	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

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Abemaciclib

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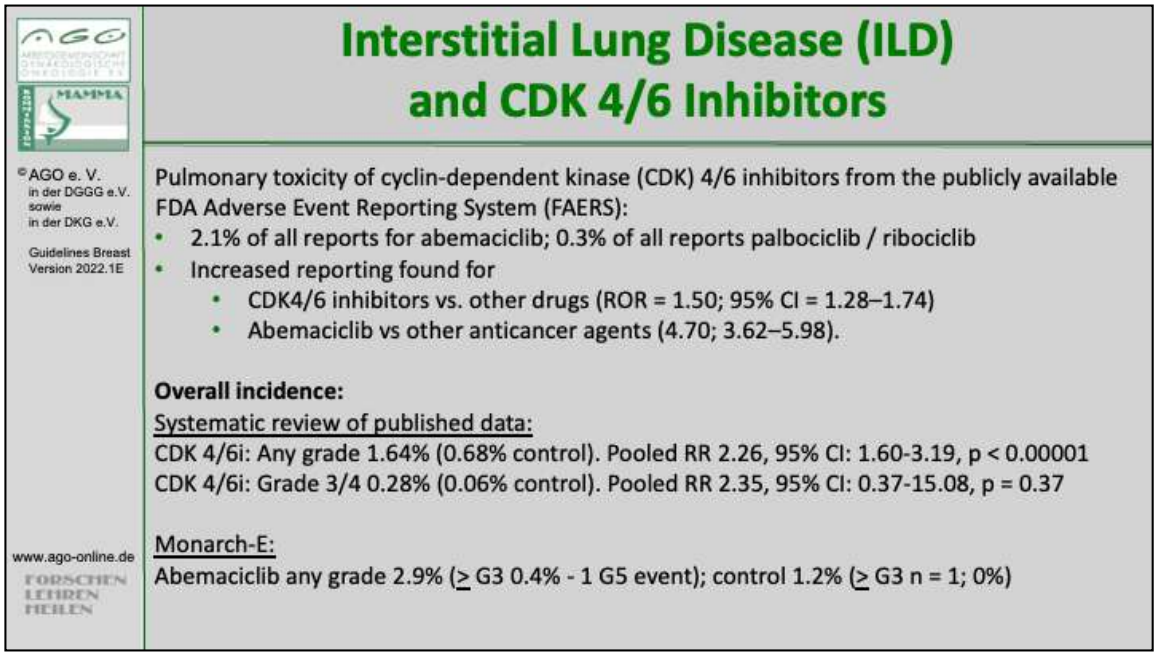

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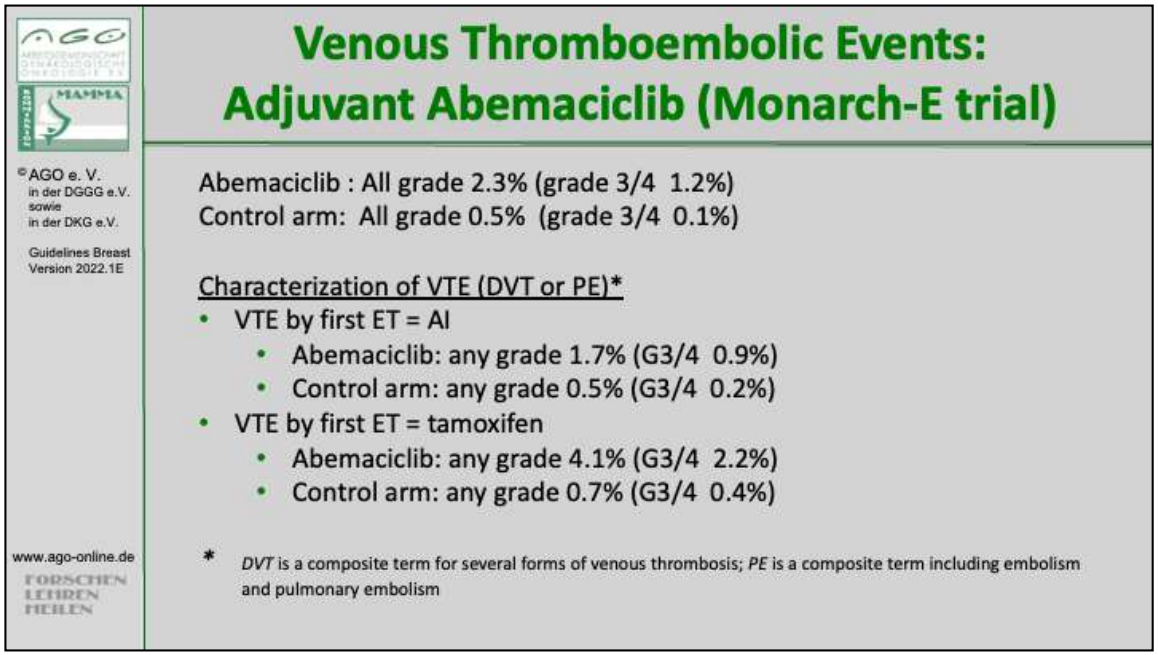

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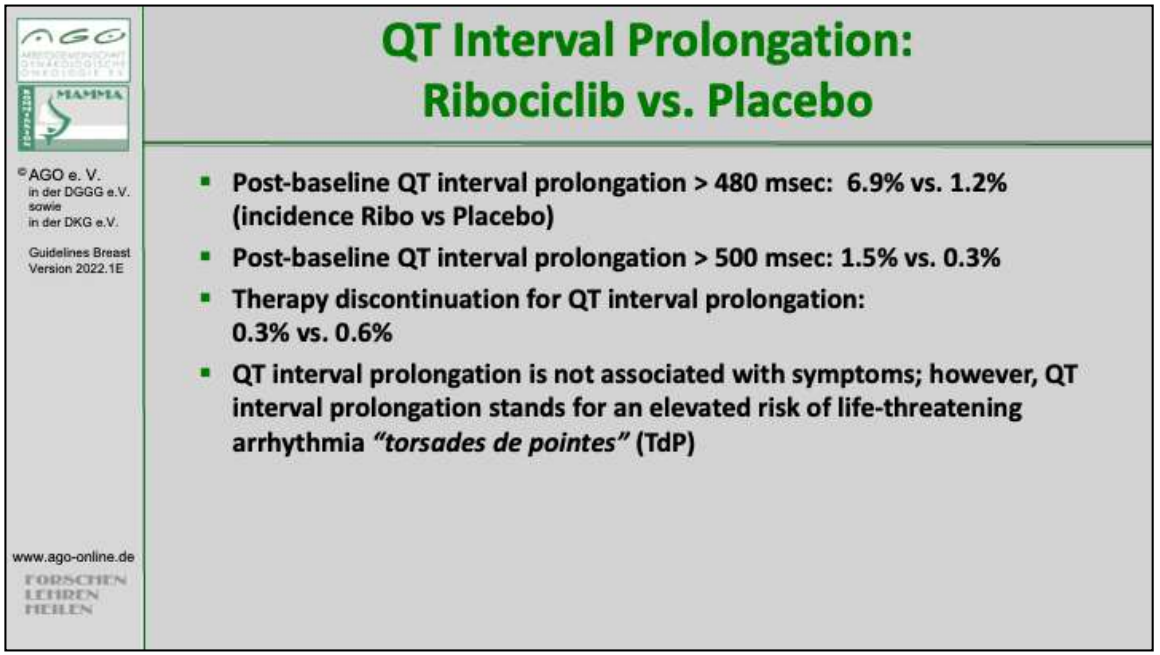

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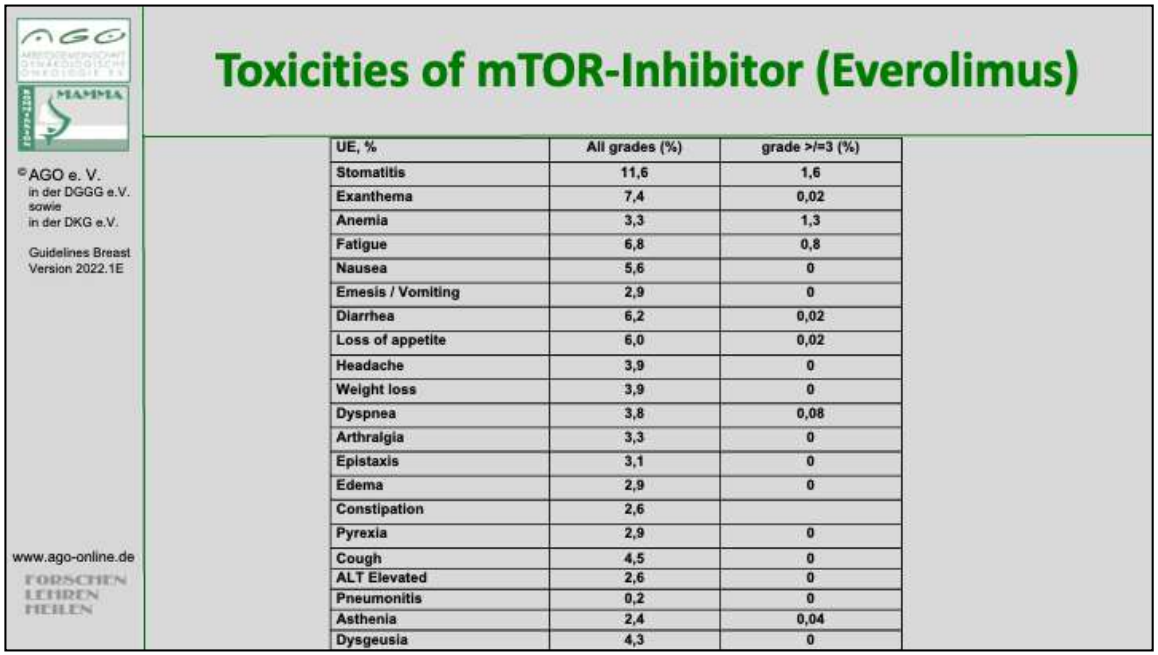

UE, %	All grades (%)	grade >/=3 (%)
Stomatitis	11,6	1,6
Exanthema	7,4	0,02
Anemia	3,3	1,3
Fatigue	6,8	0,8
Nausea	5,6	0
Emesis / Vomiting	2,9	0
Diarrhea	6,2	0,02
Loss of appetite	6,0	0,02
Headache	3,9	0
Weight loss	3,9	0
Dyspnea	3,8	0,08
Arthralgia	3,3	0
Epistaxis	3,1	0
Edema	2,9	0
Constipation	2,6	
Pyrexia	2,9	0
Cough	4,5	0
ALT Elevated	2,6	0
Pneumonitis	0,2	0
Asthenia	2,4	0,04
Dysgeusia	4,3	0

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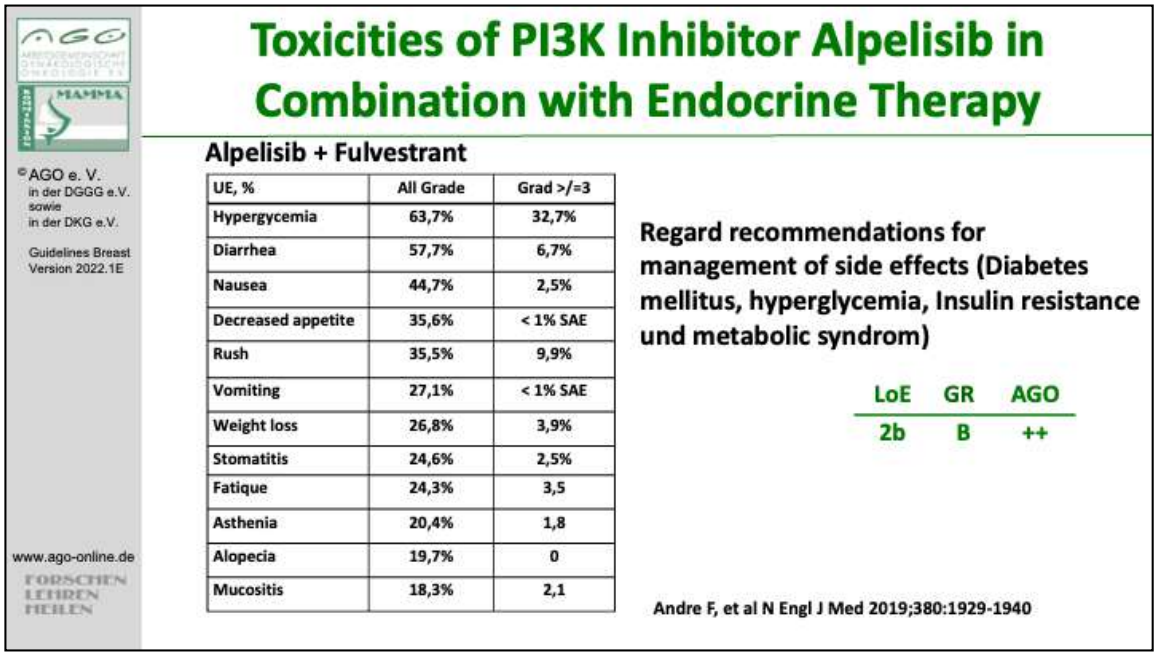

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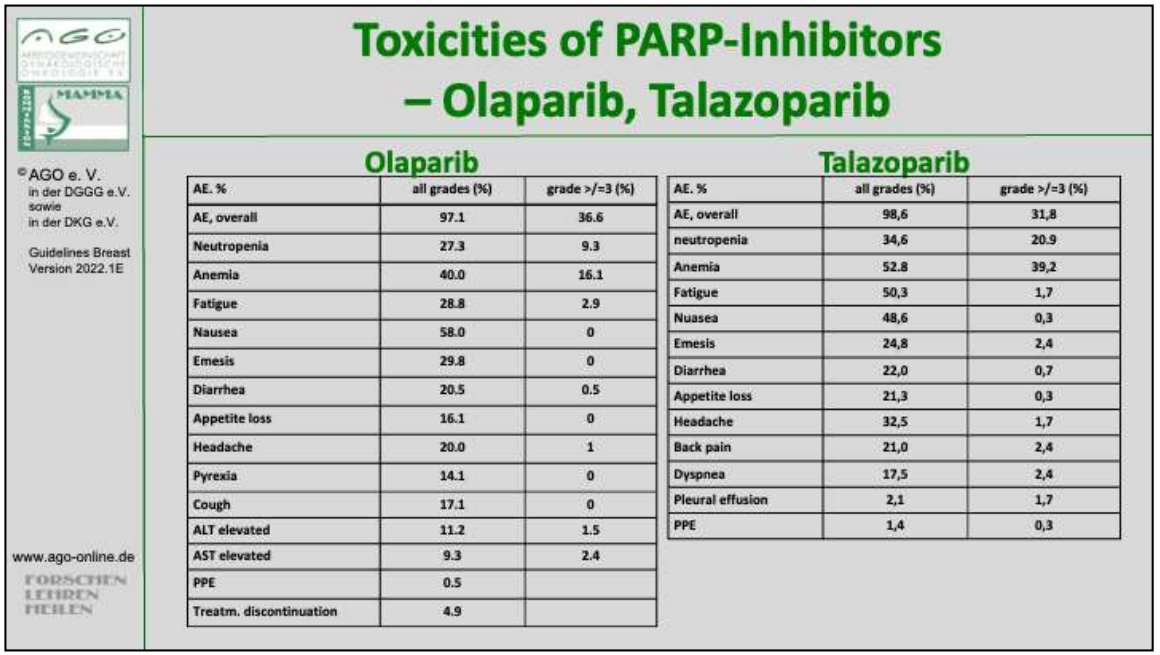

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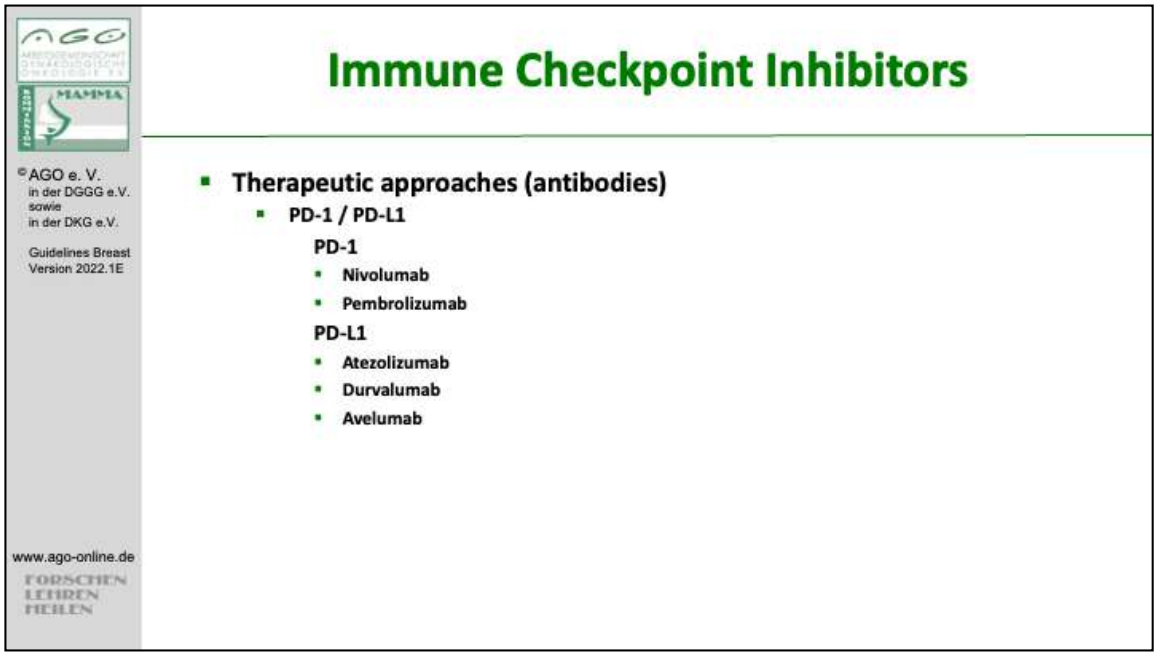

1. Haanen J, Carbonnel F, Robert C, et al, on behalf of the ESMO Guidelines Committee: Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017; 28 (suppl 4): 119-142. doi: ^0.1093/annonc/mdx225
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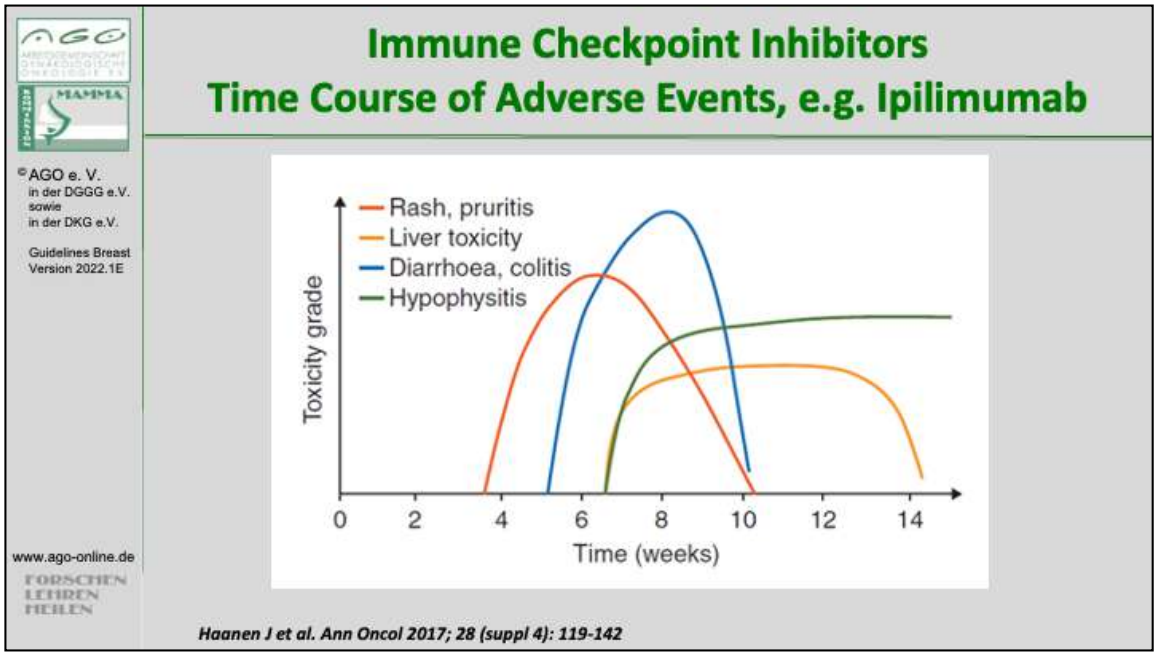

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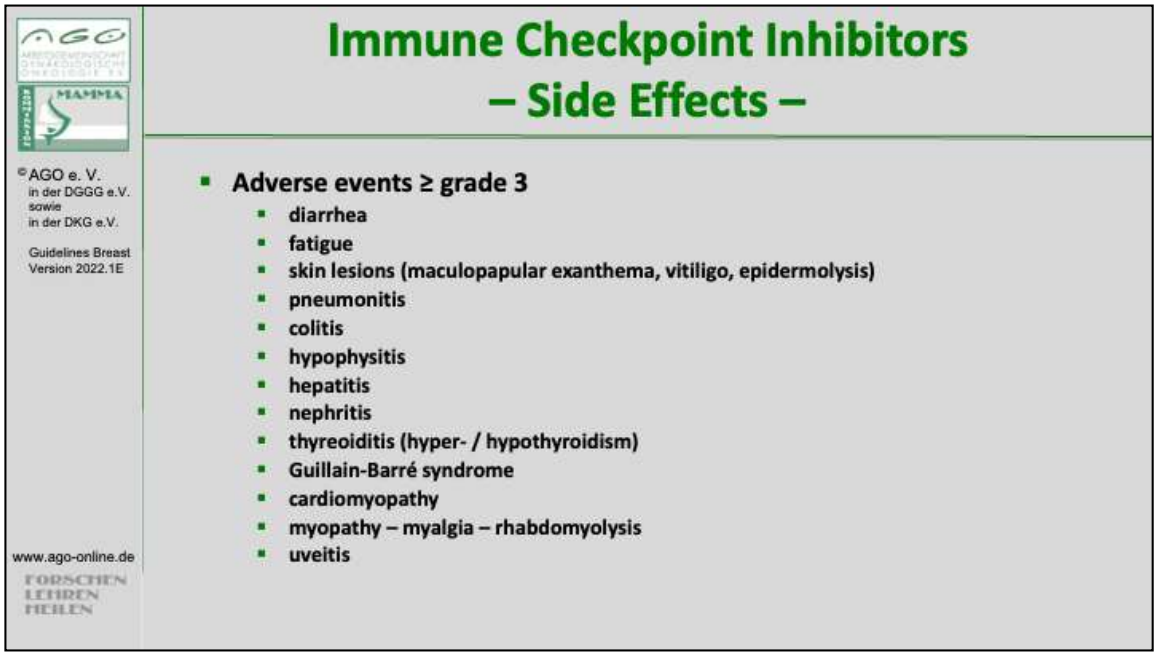

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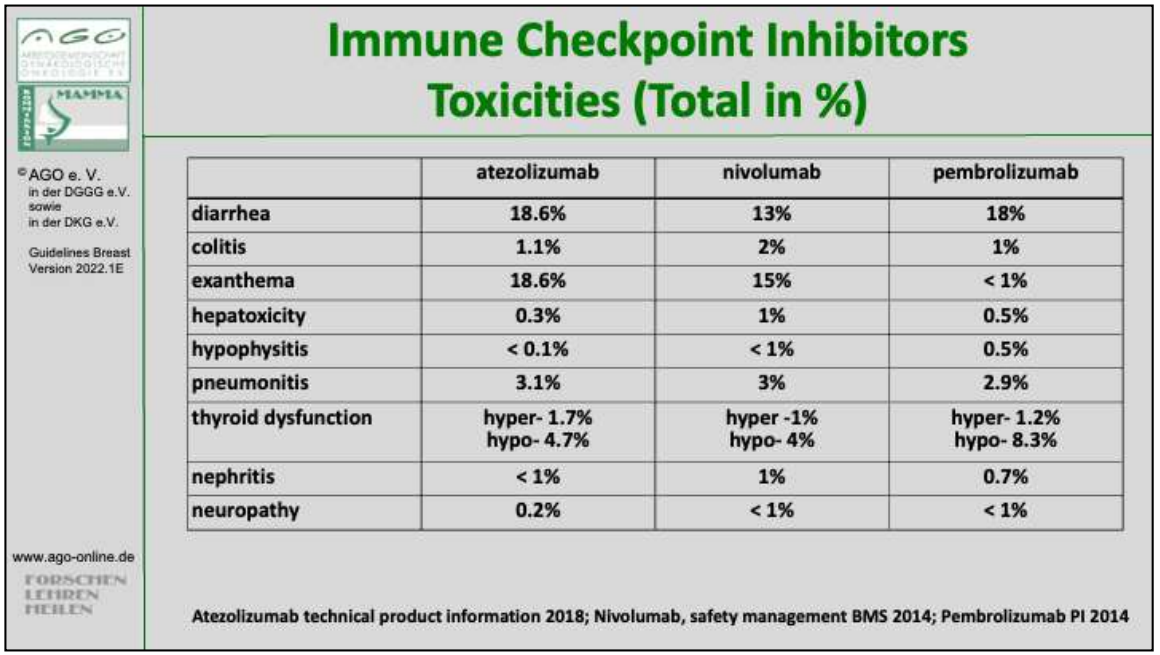
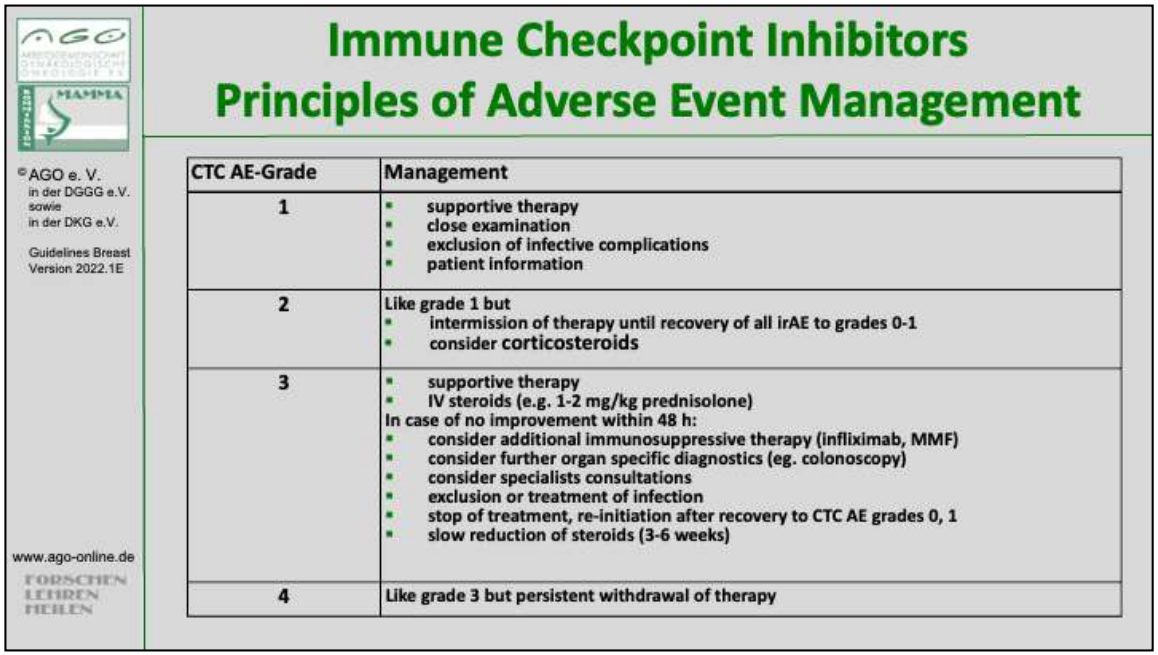


Immune Checkpoint Inhibitors Toxicities (Total in %)

	atezolizumab	nivolumab	pembrolizumab
diarrhea	18.6%	13%	18%
colitis	1.1%	2%	1%
exanthema	18.6%	15%	< 1%
hepatoxicity	0.3%	1%	0.5%
hypophysitis	< 0.1%	< 1%	0.5%
pneumonitis	3.1%	3%	2.9%
thyroid dysfunction	hyper- 1.7% hypo- 4.7%	hyper -1% hypo- 4%	hyper- 1.2% hypo- 8.3%
nephritis	< 1%	1%	0.7%
neuropathy	0.2%	< 1%	< 1%

Atezolizumab technical product information 2018; Nivolumab, safety management BMS 2014; Pembrolizumab PI 2014

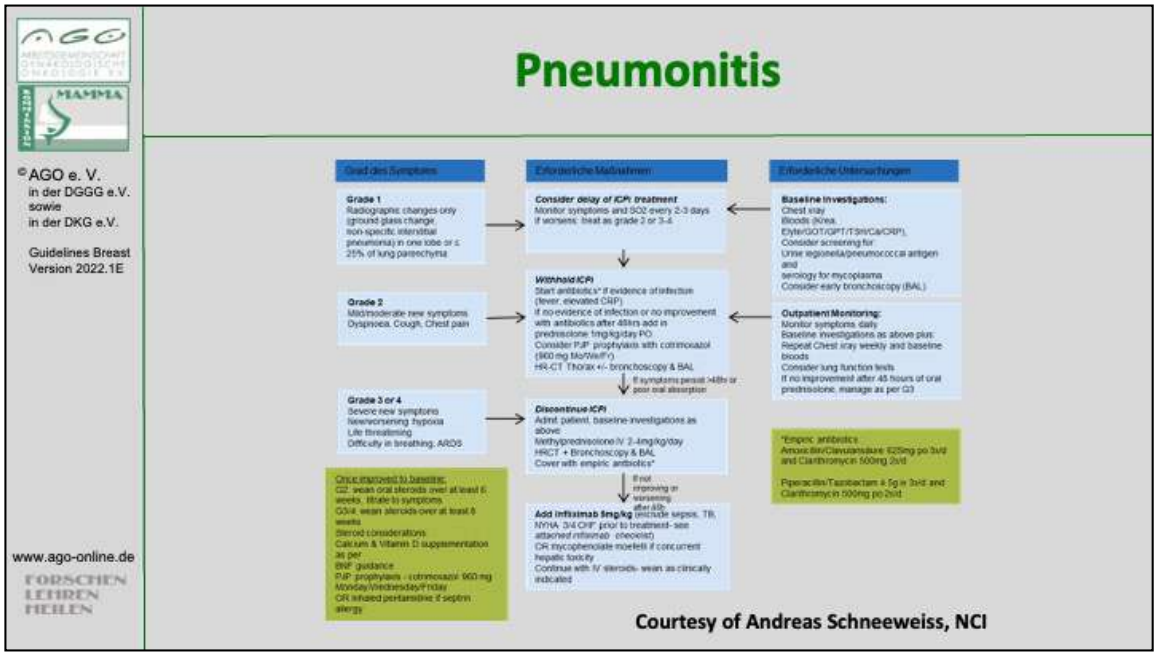
1. Atezolizumab: https://www.fachinfo.de/suche/fi/021700
2. Nivolumab: https://www.fachinfo.de/suche/fi/020675
3. Pembrolizumab: https://www.fachinfo.de/suche/fi/020716



Immune Checkpoint Inhibitors
Principles of Adverse Event Management

CTC AE-Grade	Management
1	▪ supportive therapy ▪ close examination ▪ exclusion of infective complications ▪ patient information
2	Like grade 1 but ▪ intermission of therapy until recovery of all irAE to grades 0-1 ▪ consider corticosteroids
3	▪ supportive therapy ▪ IV steroids (e.g. 1-2 mg/kg prednisolone) In case of no improvement within 48 h: ▪ consider additional immunosuppressive therapy (infliximab, MMF) ▪ consider further organ specific diagnostics (eg. colonoscopy) ▪ consider specialists consultations ▪ exclusion or treatment of infection ▪ stop of treatment, re-initiation after recovery to CTC AE grades 0, 1 ▪ slow reduction of steroids (3-6 weeks)
4	Like grade 3 but persistent withdrawal of therapy

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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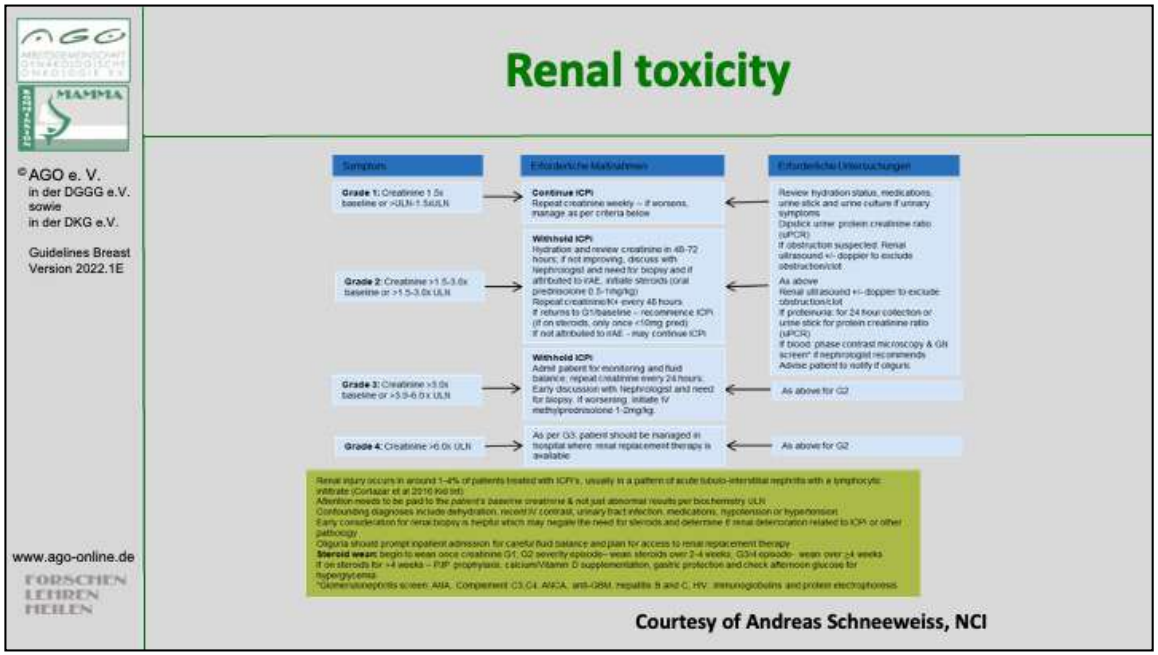

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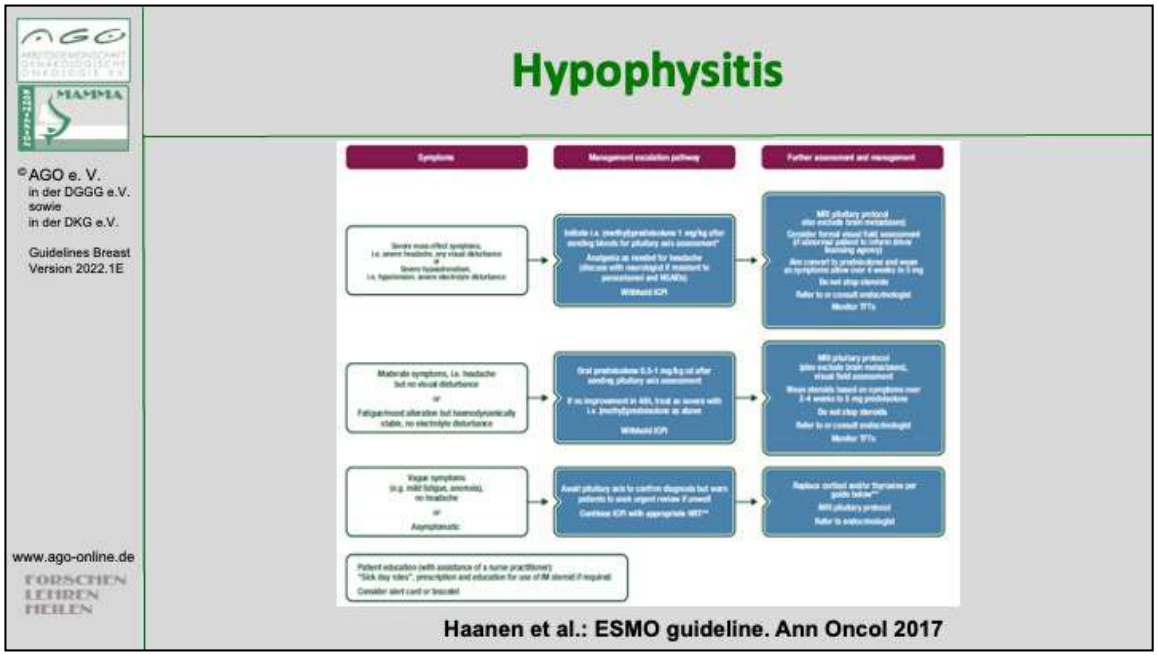

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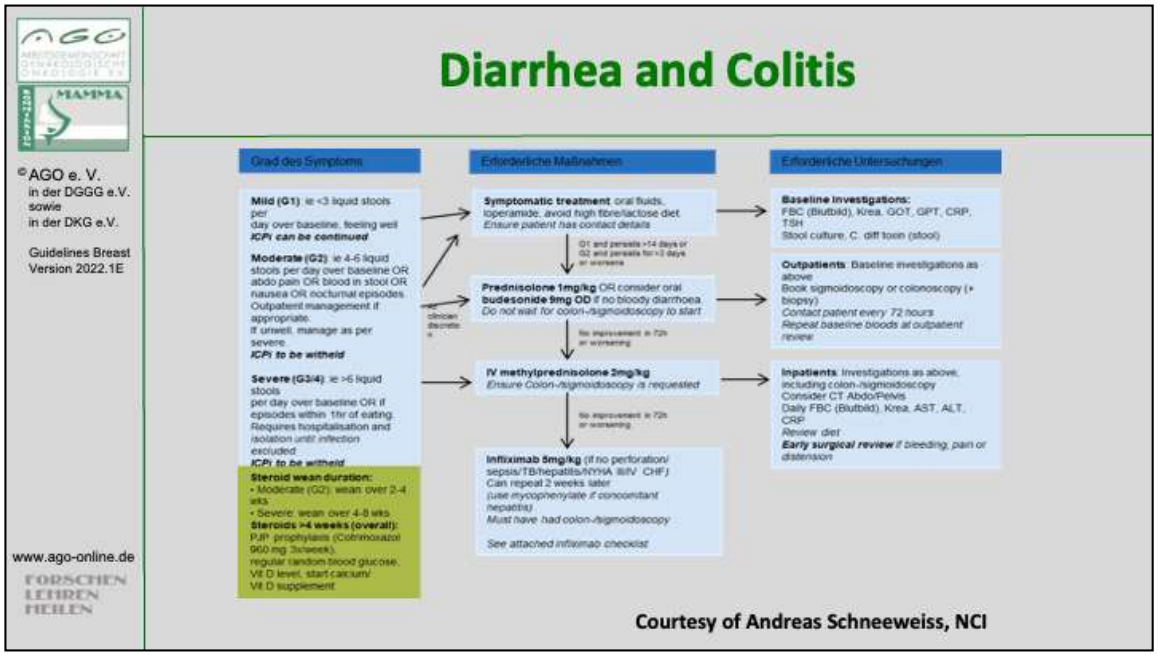

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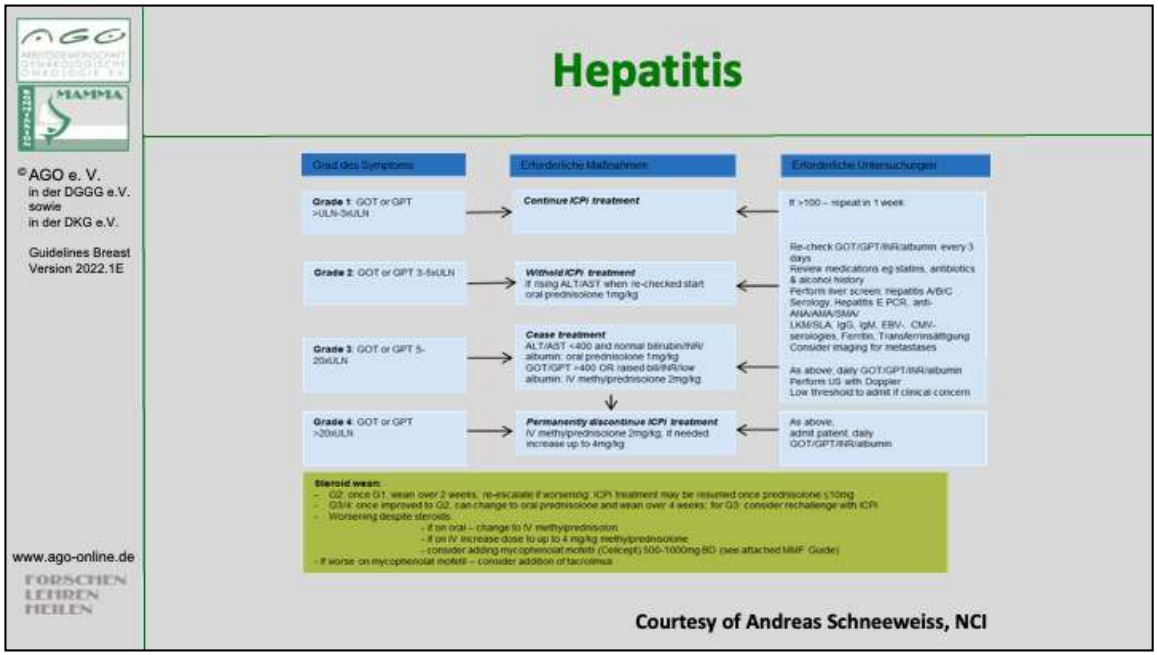

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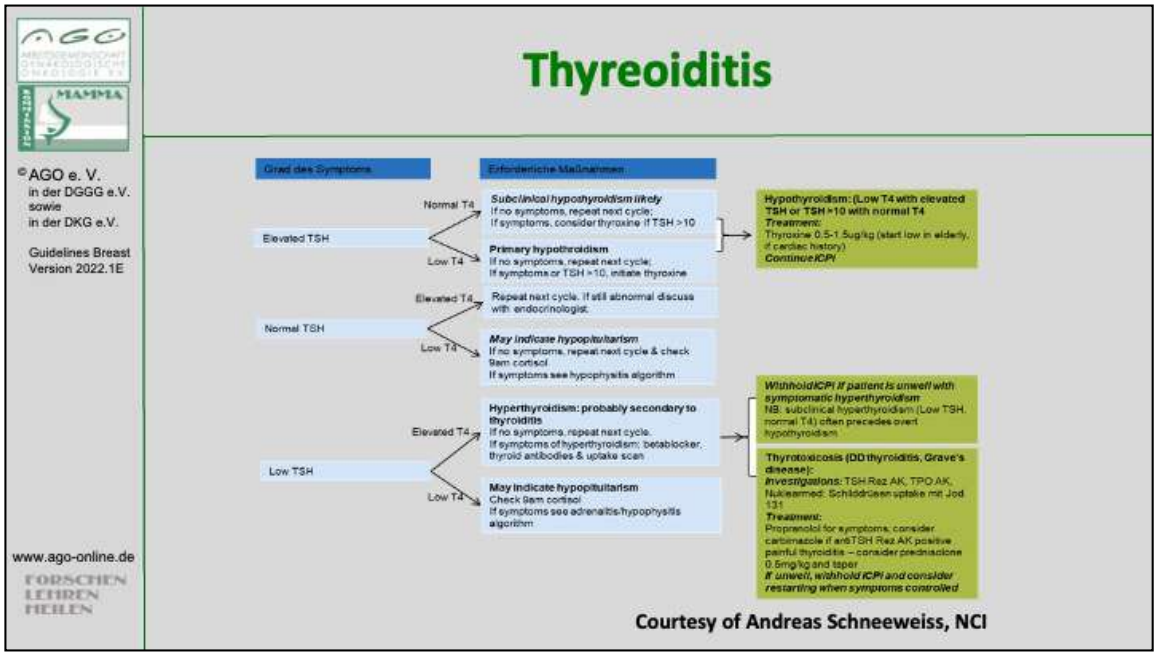

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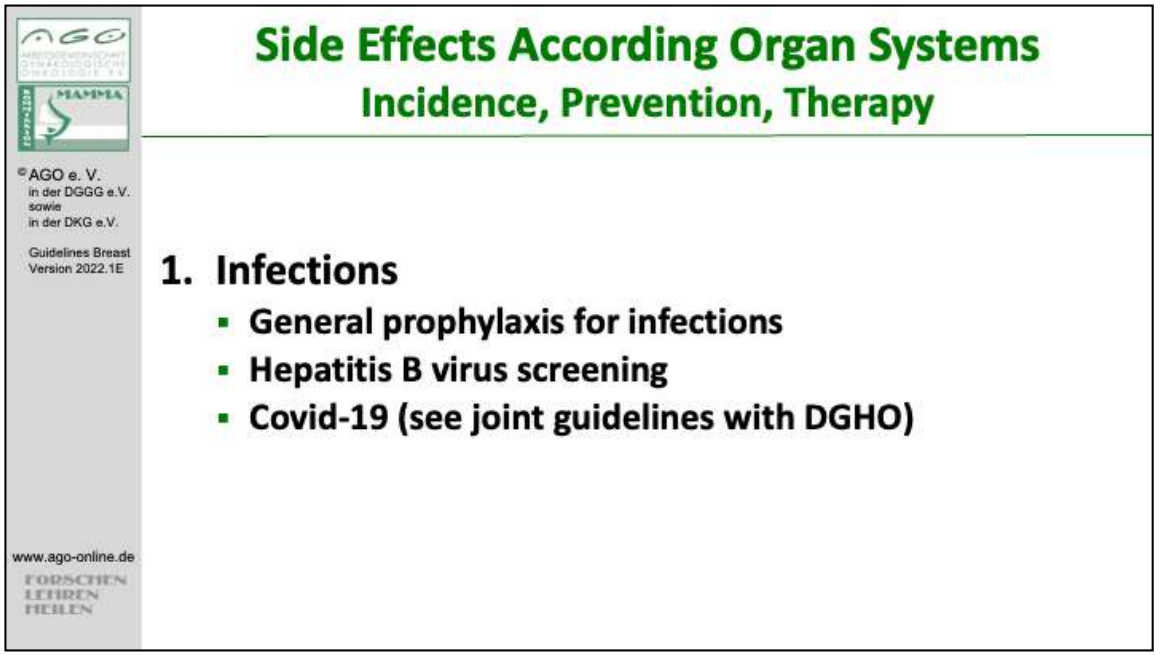

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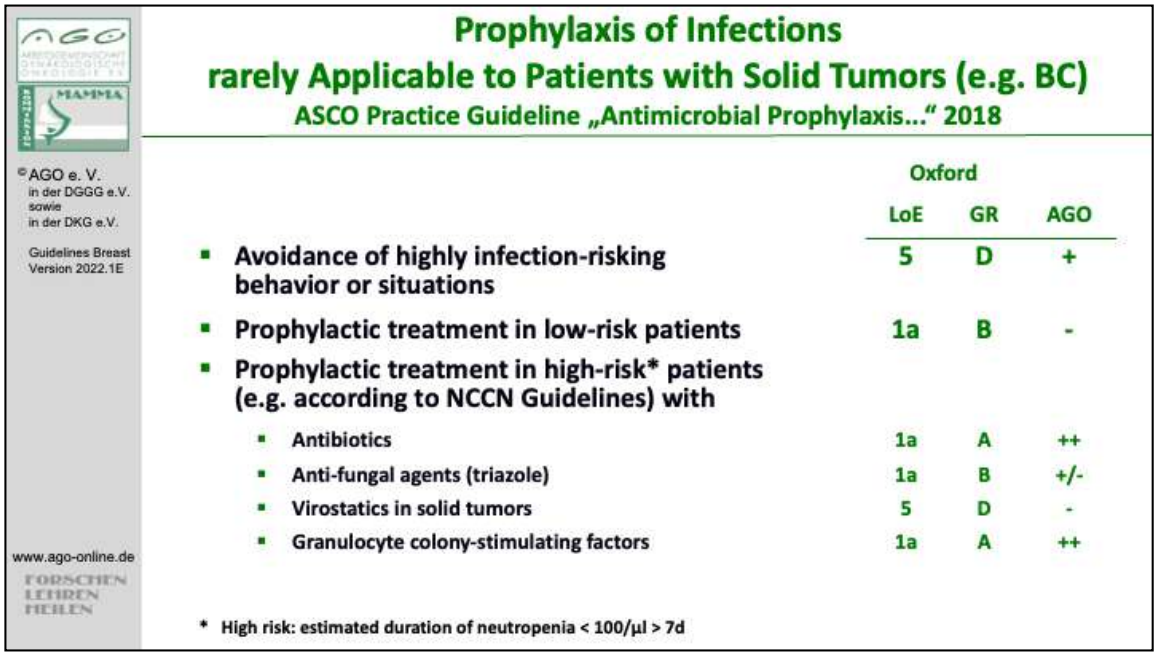

ASCO:

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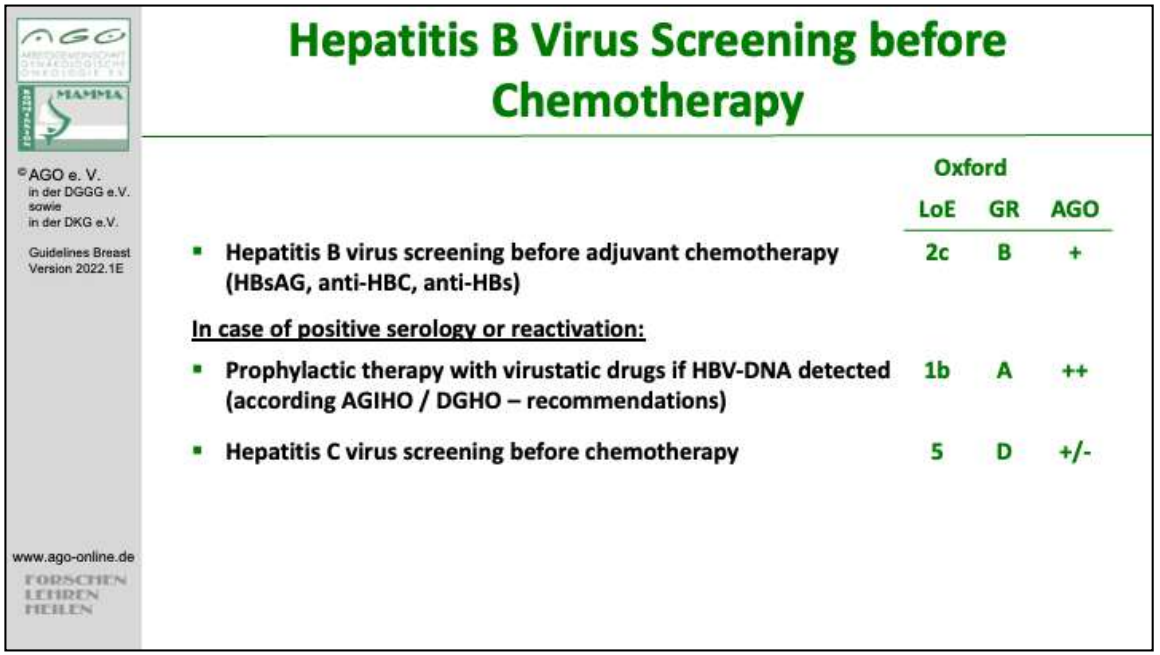

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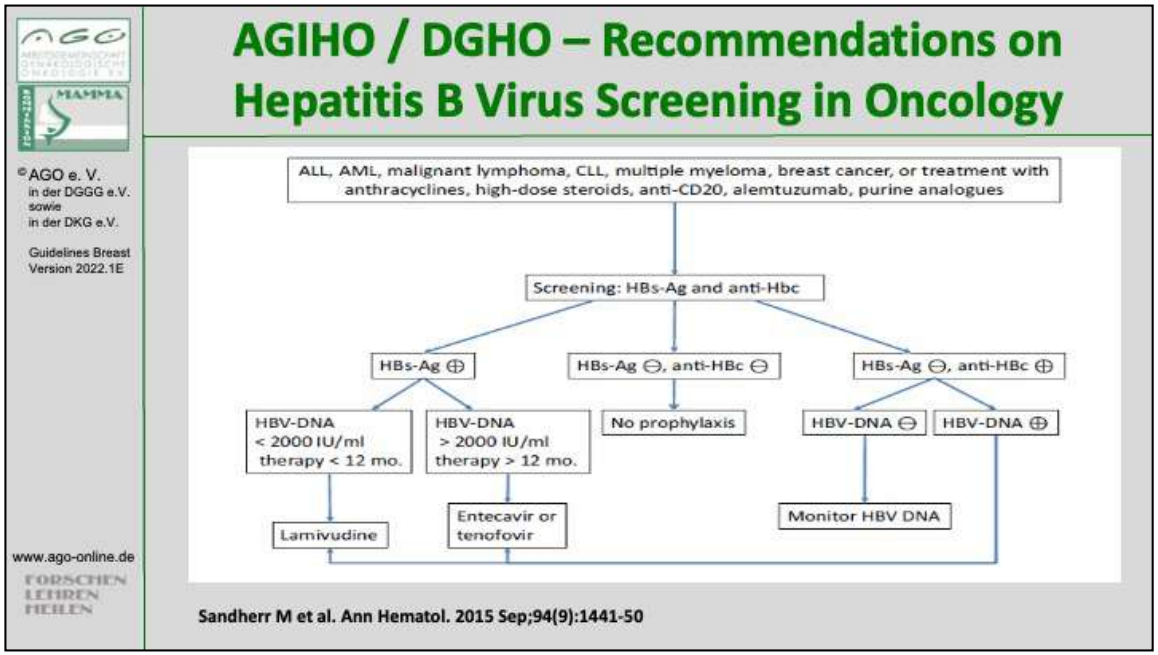

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Side Effects According Organ Systems
Incidence, Prevention, Therapy

Guidelines Breast
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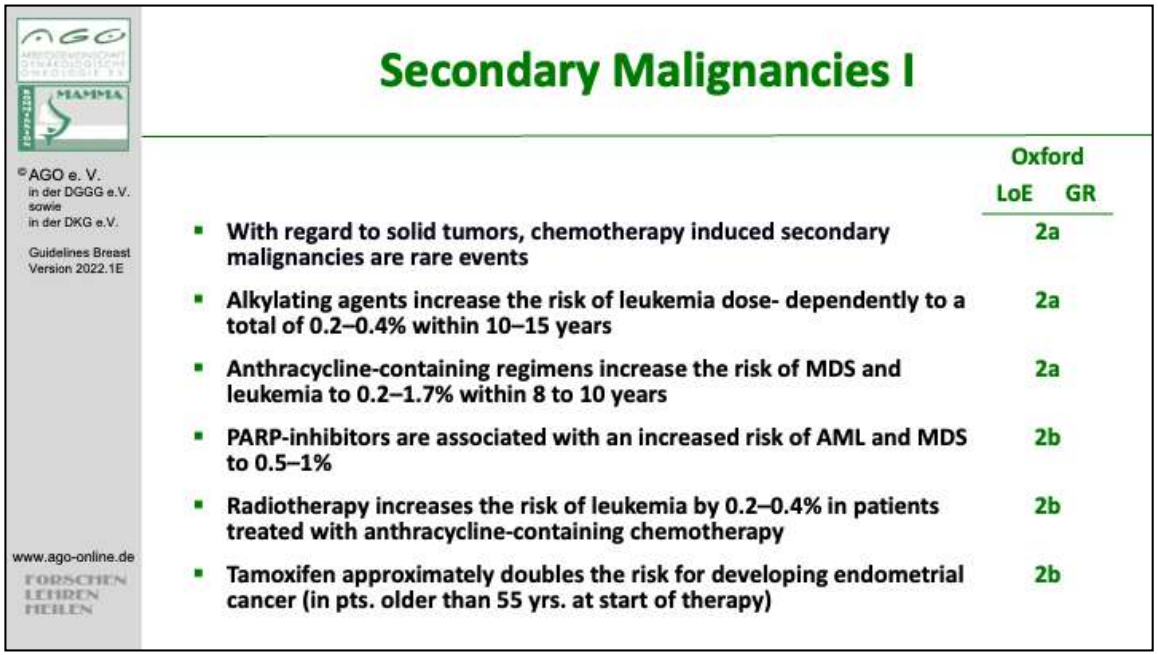
2. **Neoplasms benign, malignant and unspecified (incl. cysts and polyps)**



Statements 1-4

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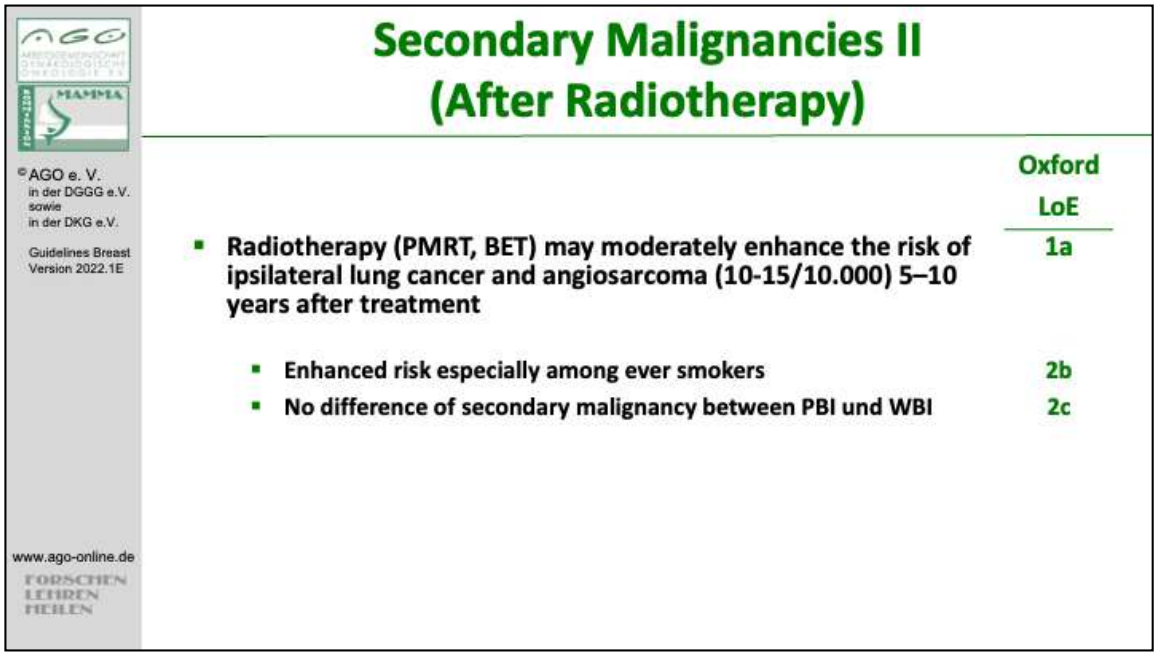

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Side Effects According Organ Systems
Incidence, Prevention, Therapy

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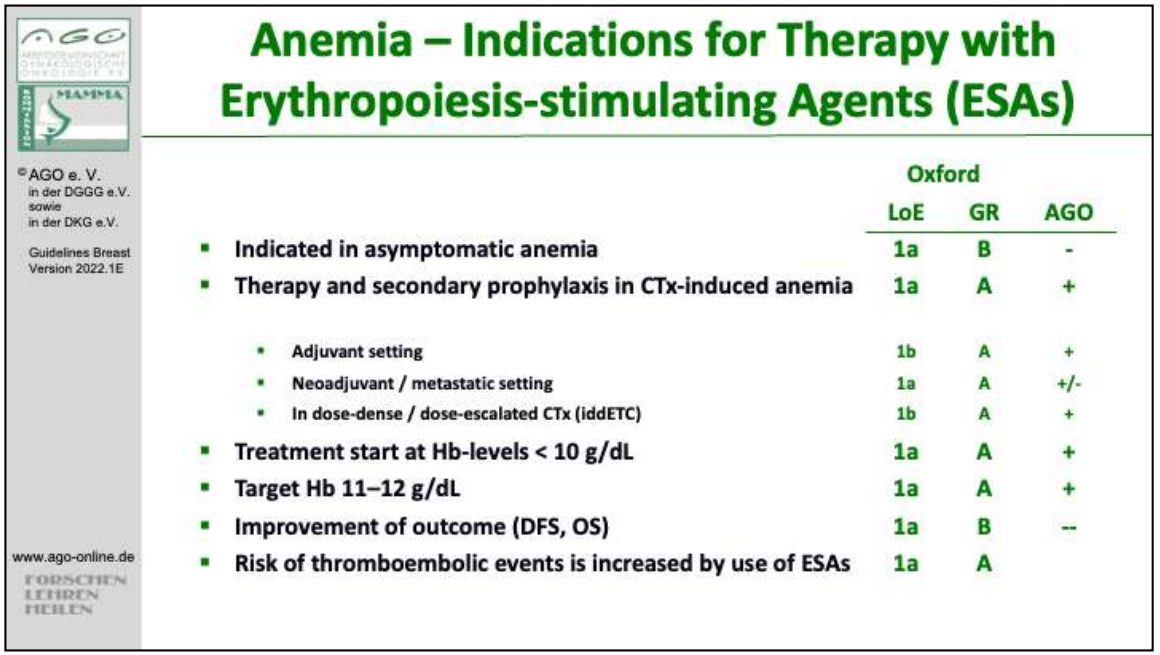
3. *Blood and Lymphatic System Disorders*

- Anemia
- Neutropenia
- Febrile Neutropenia (FN)



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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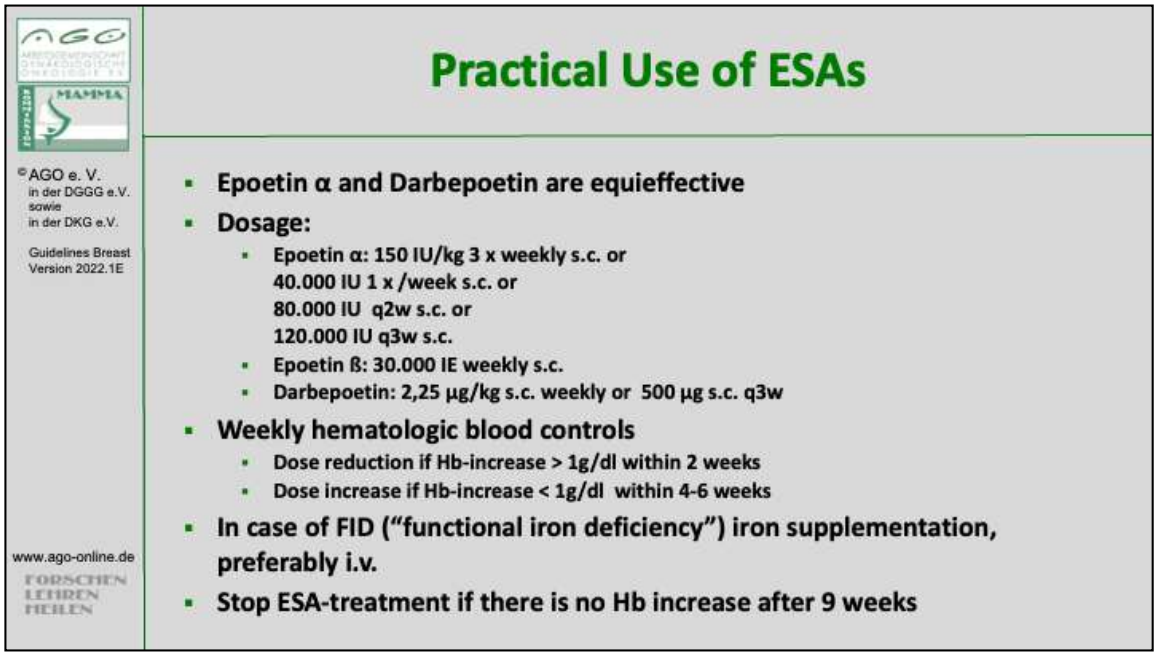

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<u>Relevant guidelines</u>

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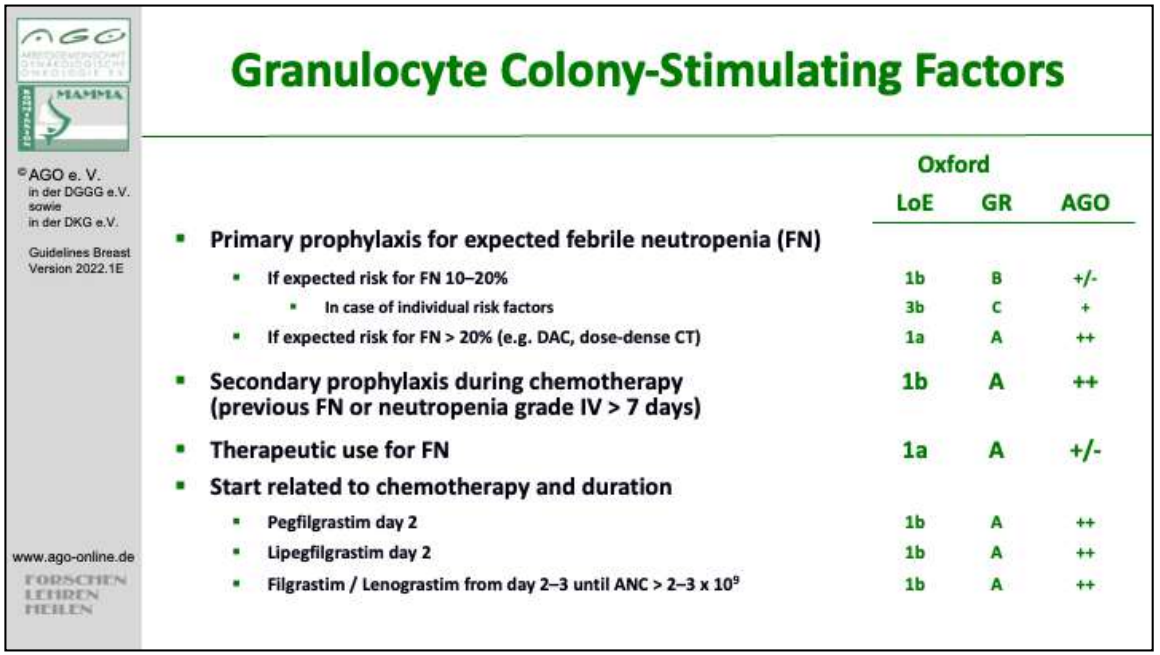

Granulocyte Colony-Stimulating Factors

	Oxford LoE	Oxford GR	AGO
▪ Primary prophylaxis for expected febrile neutropenia (FN)			
▪ If expected risk for FN 10–20%	1b	B	+/-
▪ In case of individual risk factors	3b	C	+
▪ If expected risk for FN > 20% (e.g. DAC, dose-dense CT)	1a	A	++
▪ Secondary prophylaxis during chemotherapy (previous FN or neutropenia grade IV > 7 days)	1b	A	++
▪ Therapeutic use for FN	1a	A	+/-
▪ Start related to chemotherapy and duration			
▪ Pegfilgrastim day 2	1b	A	++
▪ Lipegfilgrastim day 2	1b	A	++
▪ Filgrastim / Lenograstim from day 2–3 until ANC > 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
2. NCCN Guidelines 1.2022
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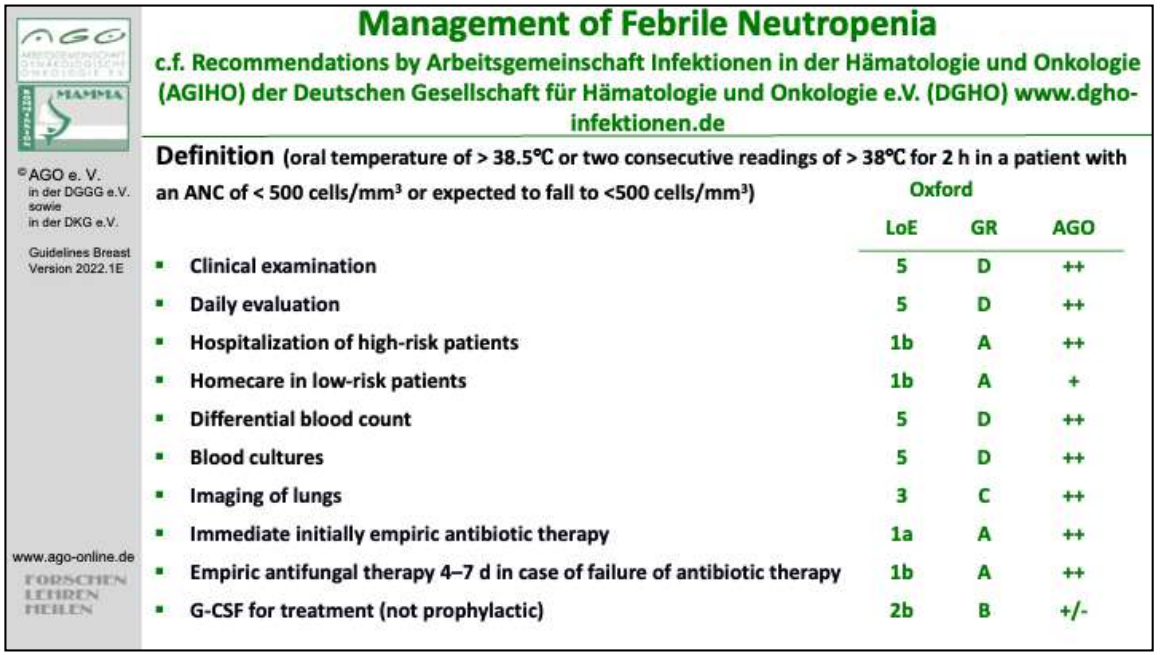

Management of Febrile Neutropenia

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

Guidelines Breast
Version 2022.1E

Definition (oral temperature of > 38.5°C or two consecutive readings of > 38°C for 2 h in a patient with an ANC of < 500 cells/mm³ or expected to fall to <500 cells/mm³)

	Oxford		
	LoE	GR	AGO
▪ Clinical examination	5	D	++
▪ Daily evaluation	5	D	++
▪ Hospitalization of high-risk patients	1b	A	++
▪ Homecare in low-risk patients	1b	A	+
▪ Differential blood count	5	D	++
▪ Blood cultures	5	D	++
▪ Imaging of lungs	3	C	++
▪ Immediate initially empiric antibiotic therapy	1a	A	++
▪ Empiric antifungal therapy 4–7 d in case of failure of antibiotic therapy	1b	A	++
▪ G-CSF for treatment (not prophylactic)	2b	B	+/-

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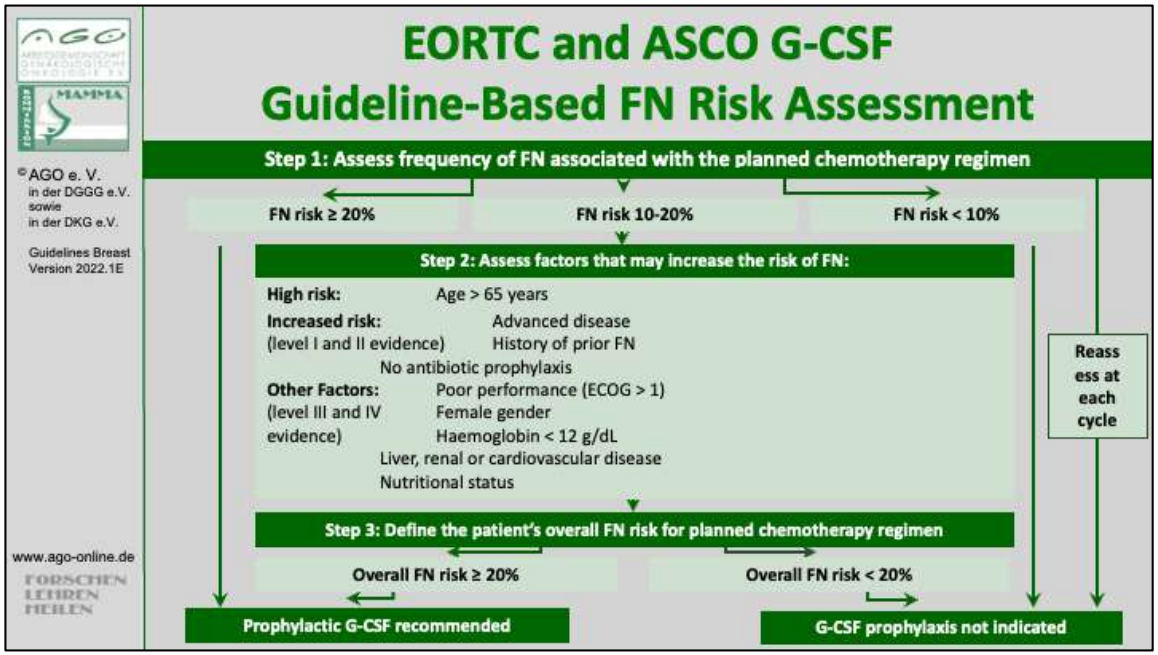

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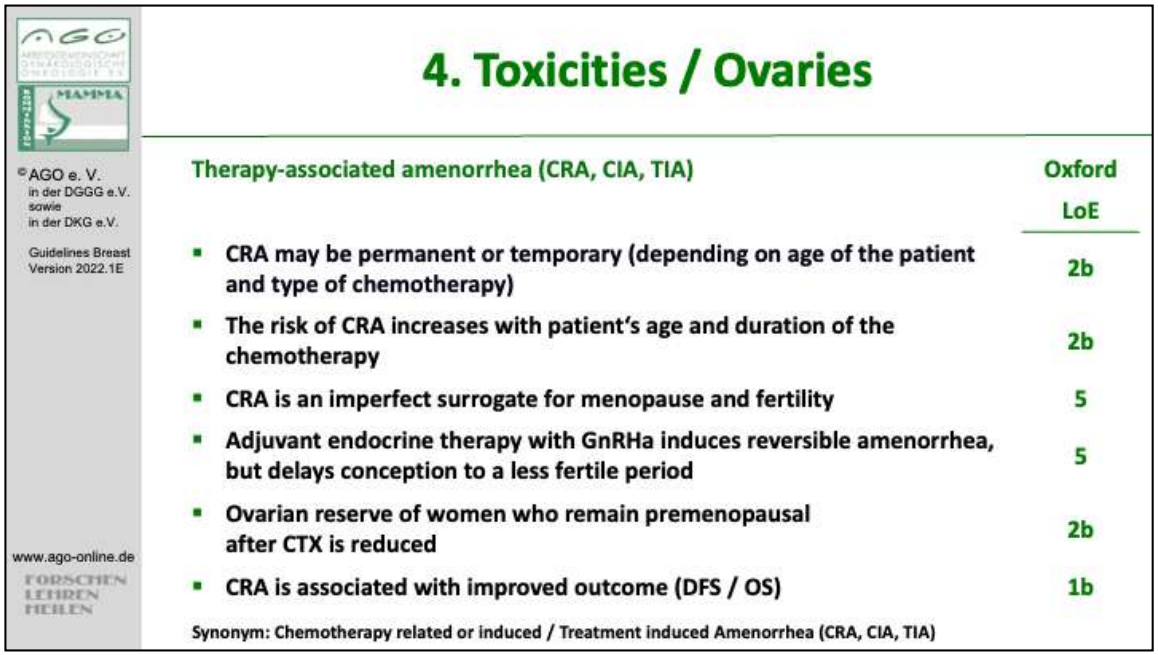

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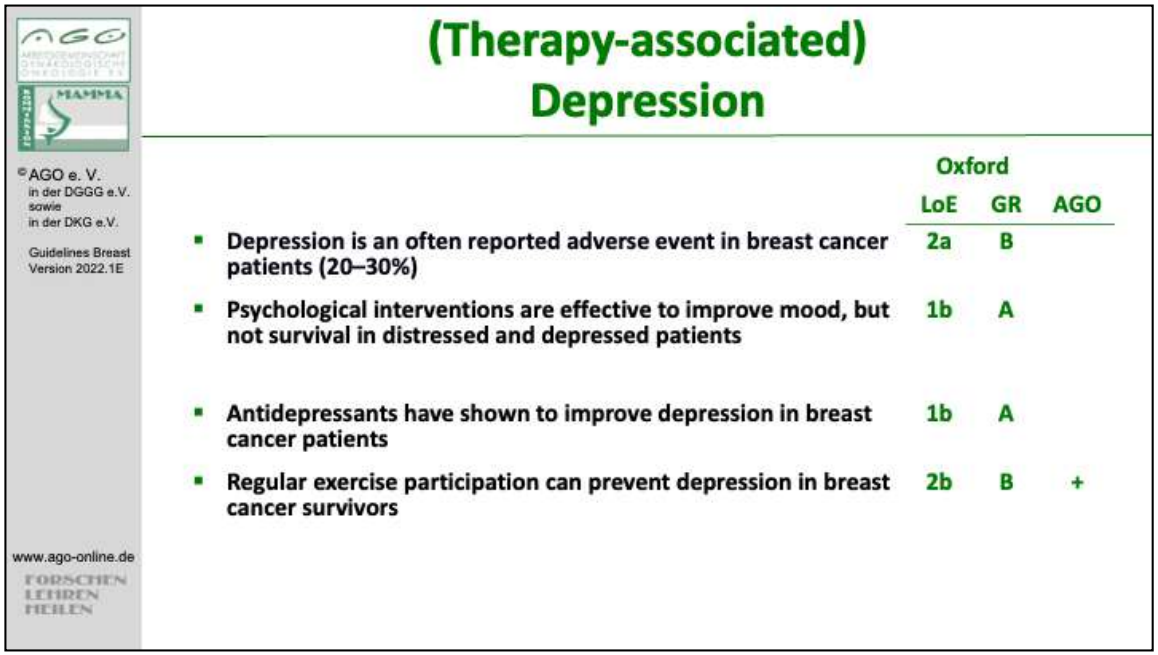
Side Effects According Organ Systems
Incidence, Prevention, Therapy

5. Psychiatric Disorders

- Depression
- Fatigue
- Cognitive impairment
- Sleep disturbances



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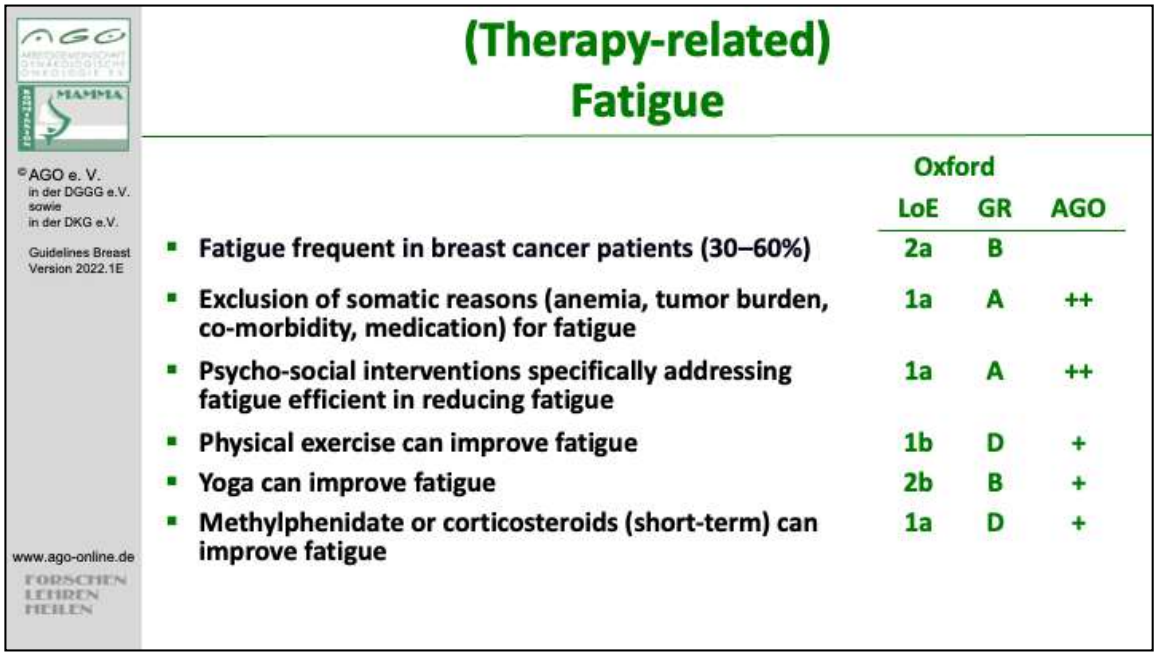

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Fatigue is frequently present…

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Methylphenidate…

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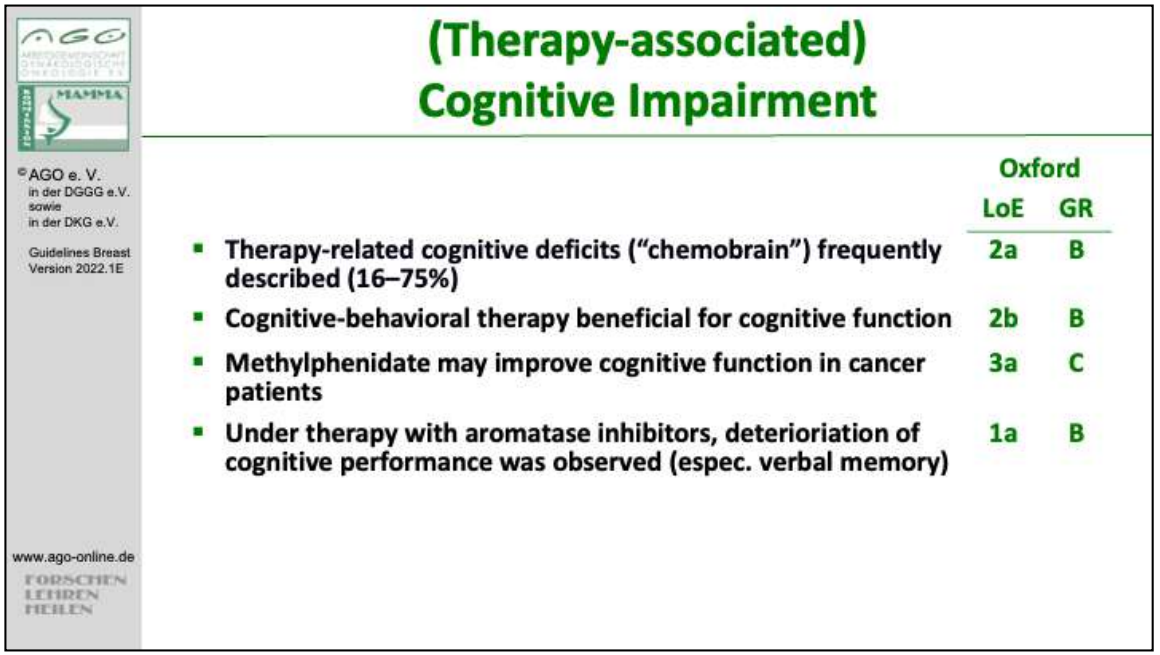

<u>Therapiebedingte kognitive Störungen (sog. „Chemobrain“) häufig beschrieben</u>

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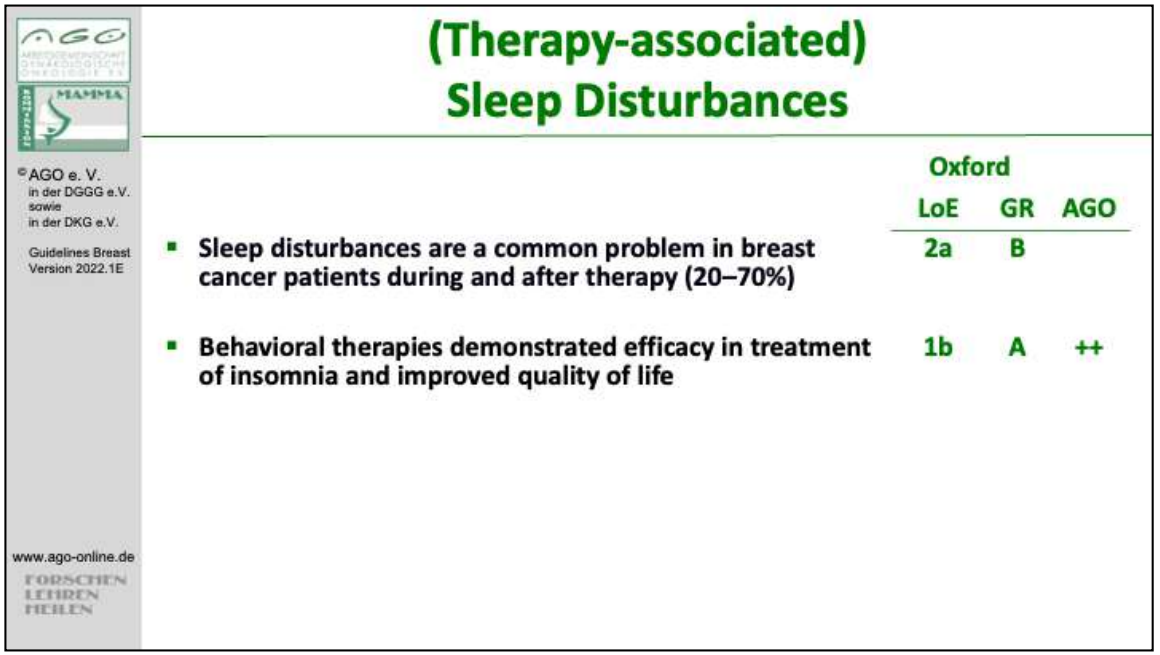

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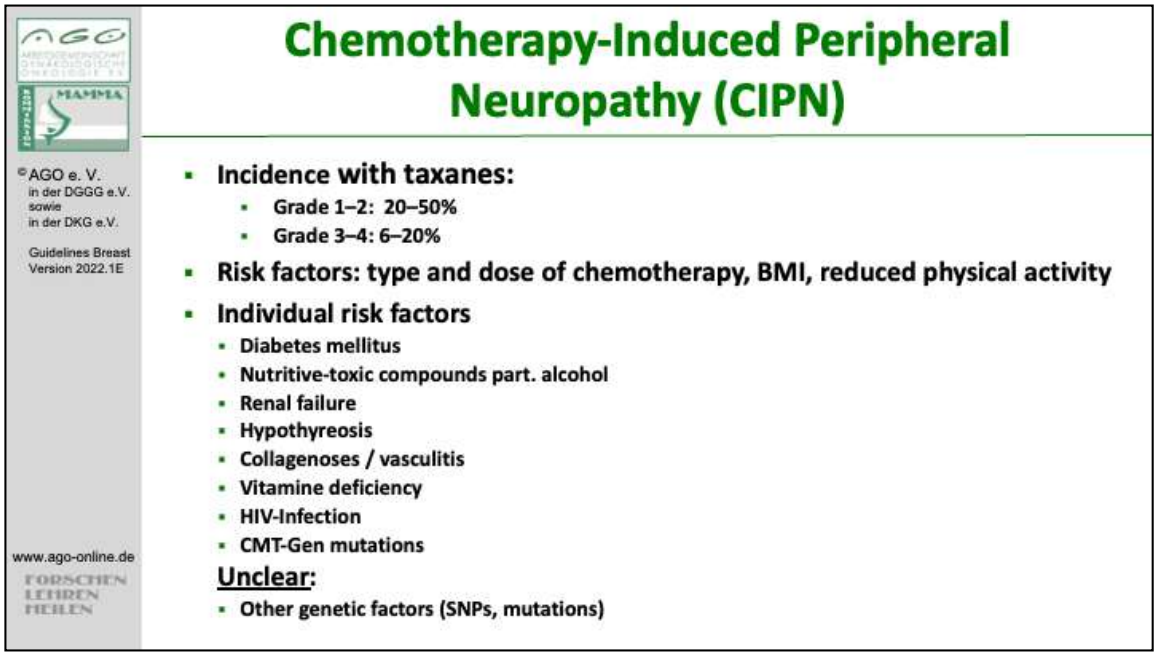
Side Effects According Organ Systems
Incidence, Prevention, Therapy

6. Nervous system disorders

- **Chemotherapy-Induced Peripheral Neuropathy (CIPN)**



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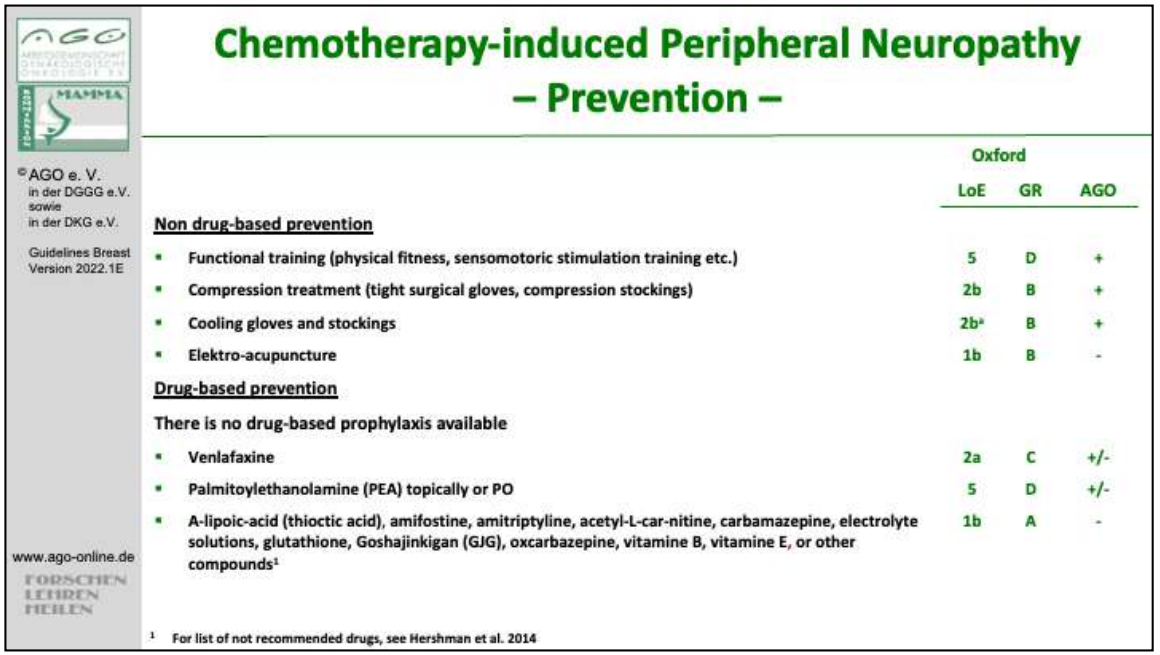

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Drug-based prevention

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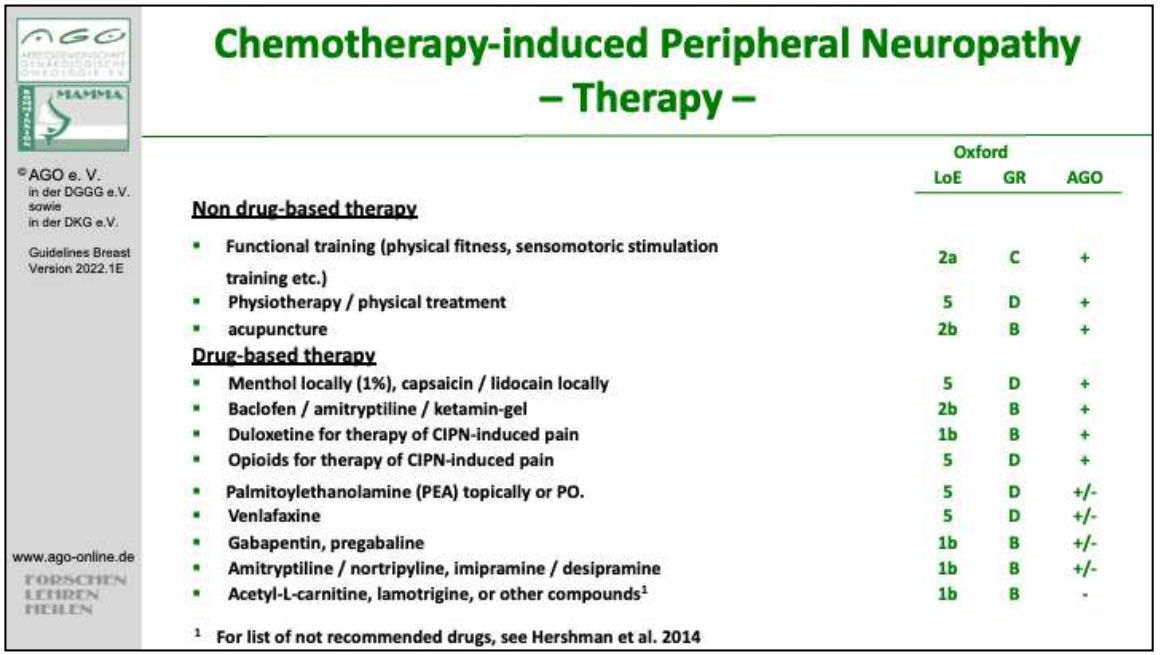

Chemotherapy-induced Peripheral Neuropathy – Therapy –

Guidelines Breast
Version 2022.1E

	Oxford LoE	Oxford GR	AGO
Non drug-based therapy			
▪ Functional training (physical fitness, sensomotoric stimulation training etc.)	2a	C	+
▪ Physiotherapy / physical treatment	5	D	+
▪ acupuncture	2b	B	+
Drug-based therapy			
▪ Menthol locally (1%), capsaicin / lidocain locally	5	D	+
▪ Baclofen / amitryptiline / ketamin-gel	2b	B	+
▪ Duloxetine for therapy of CIPN-induced pain	1b	B	+
▪ Opioids for therapy of CIPN-induced pain	5	D	+
▪ Palmitoylethanolamine (PEA) topically or PO.	5	D	+/-
▪ Venlafaxine	5	D	+/-
▪ Gabapentin, pregabaline	1b	B	+/-
▪ Amitryptiline / nortripyline, imipramine / desipramine	1b	B	+/-
▪ Acetyl-L-carnitine, lamotrigine, or other compounds[1]	1b	B	-

[1] For list of not recommended drugs, see Hershman et al. 2014

Reviews / Leitlinien

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Nicht-medikamentöse Therapie

Funktionstraining

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Medikamentöse Therapie

Menthol / Capsaicin

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Akupunktur:
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Side Effects According Organ Systems
Incidence, Prevention, Therapy

Guidelines Breast
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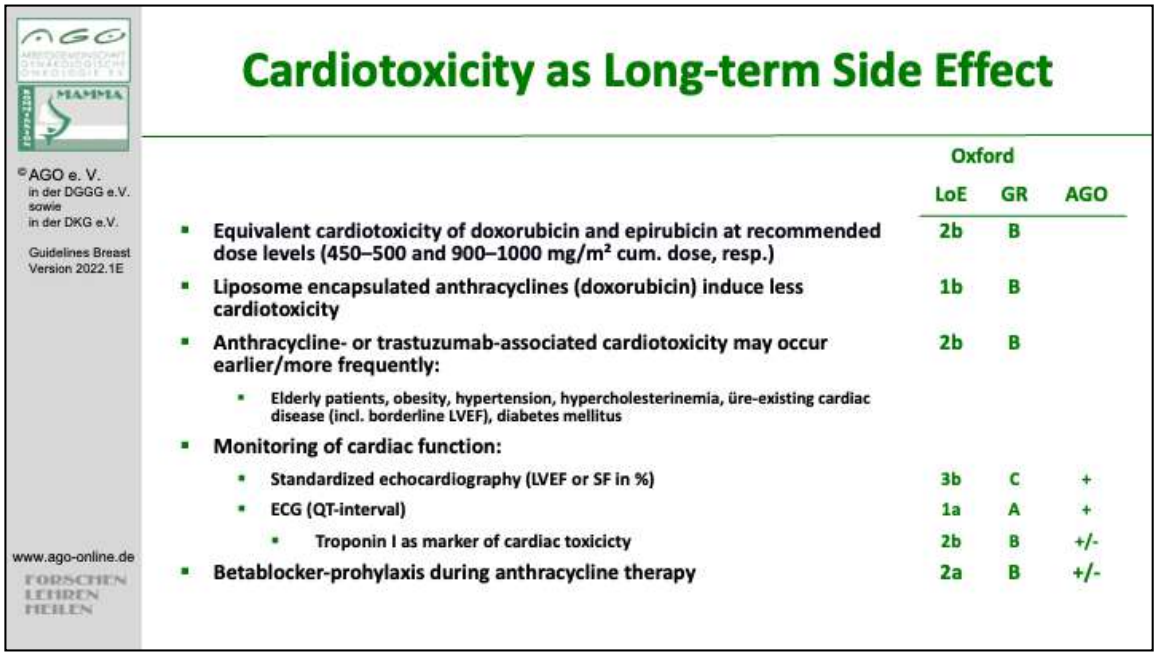
7. Cardiac Disorders



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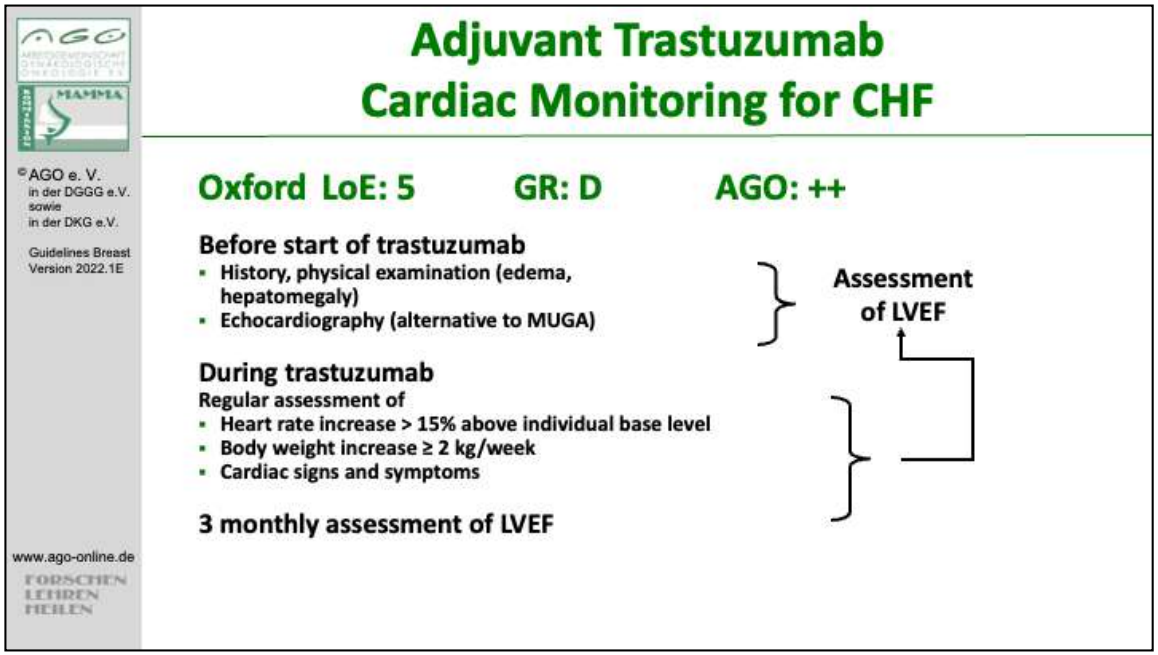

Statement: Cardiac Monitoring (5 D ++)

Vote result of the AGO recommendation: 100%

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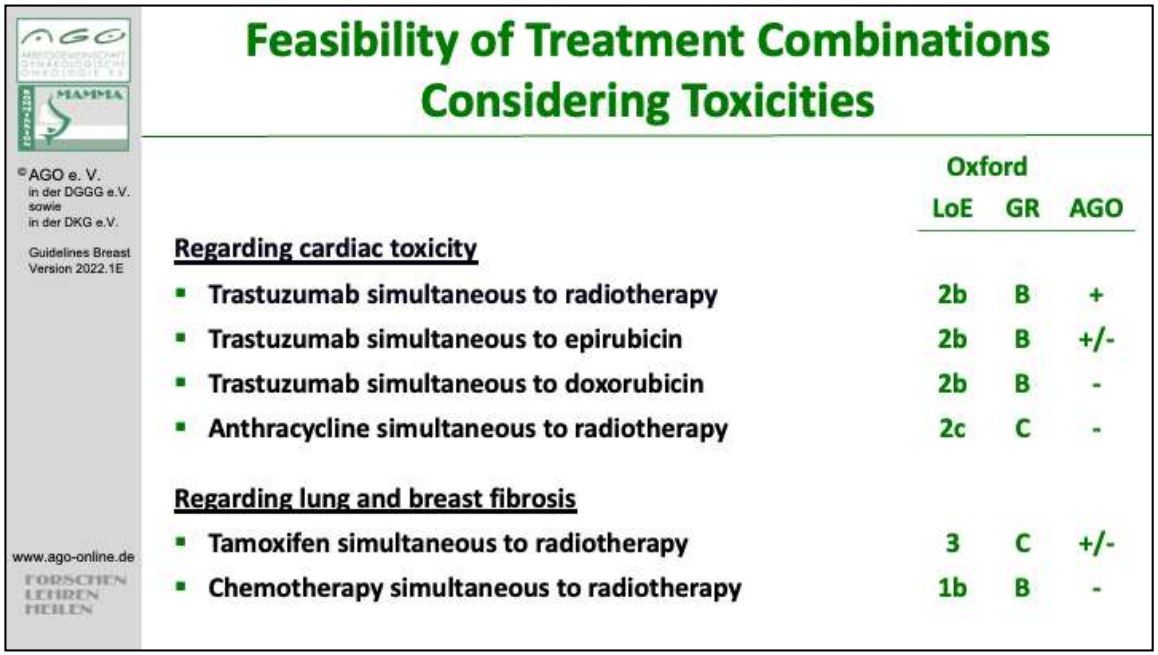

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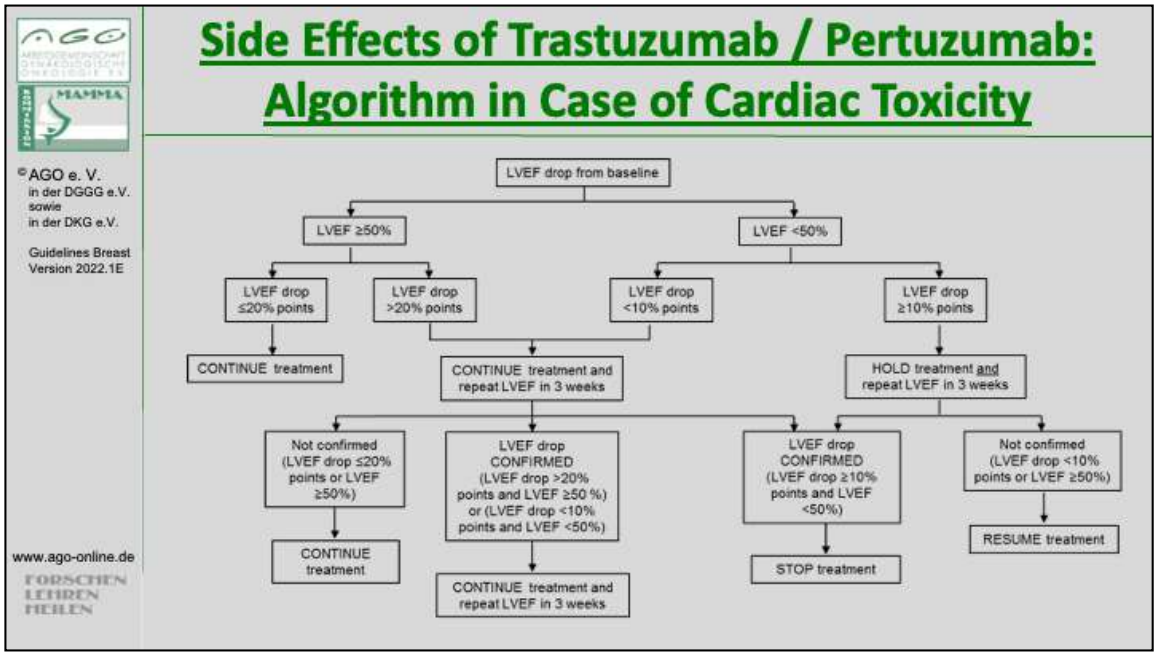

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Side Effects According Organ Systems
Incidence, Prevention, Therapy

Guidelines Breast
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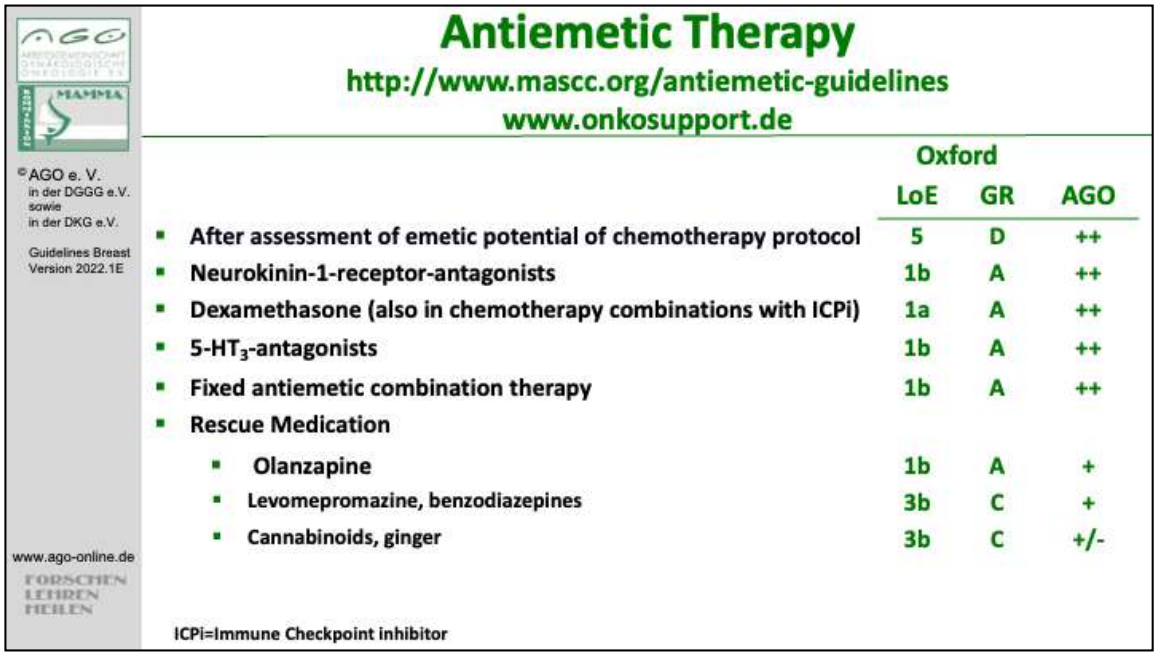
8. Gastrointestinal Disorders

- Nausea, Emesis
- Mucositis
  - Stomatitis (Everolimus)
- Diarrhea
- Constipation



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Olanzapine

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Antiemetic Therapy
https://www.mascc.org/antiemetic-guidelines

Guidelines Breast
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www.ago-online.de
FORSCHEN
LEHREN
HEILEN

ACUTE Nausea and Vomiting: SUMMARY

EMETIC RISK GROUP	ANTIEMETICS
High Non-AC	5-HT$_3$ + DEX + NK$_1$ +/- OLZ*
High AC	5-HT$_3$ + DEX + NK$_1$ +/- OLZ*
Carboplatin	5-HT$_3$ + DEX + NK$_1$
Moderate (other than carboplatin)	5-HT$_3$ + DEX
Low	5-HT$_3$ or DEX or DOP
Minimal	No routine prophylaxis

5-HT$_3$ = serotonin$_3$ receptor antagonist | DEX = DEXAMETHASONE | NK$_1$ = neurokinin$_1$ receptor antagonist such as APREPITANT or FOSAPREPITANT or ROLAPITANT or NEPA (combination of netupitant and palonosetron) | OLZ = OLANZAPINE | DOP = dopamine receptor antagonist

NOTE: If the NK$_1$ receptor antagonist is not available for AC chemotherapy, palonosetron is the preferred 5-HT$_3$ receptor antagonist.

* OLZ: Olanzapine may be added particularly if nausea is a concern.

Multinational Association of Supportive Care in Cancer
Supportive Care Modes Excellent Cancer Care Possible

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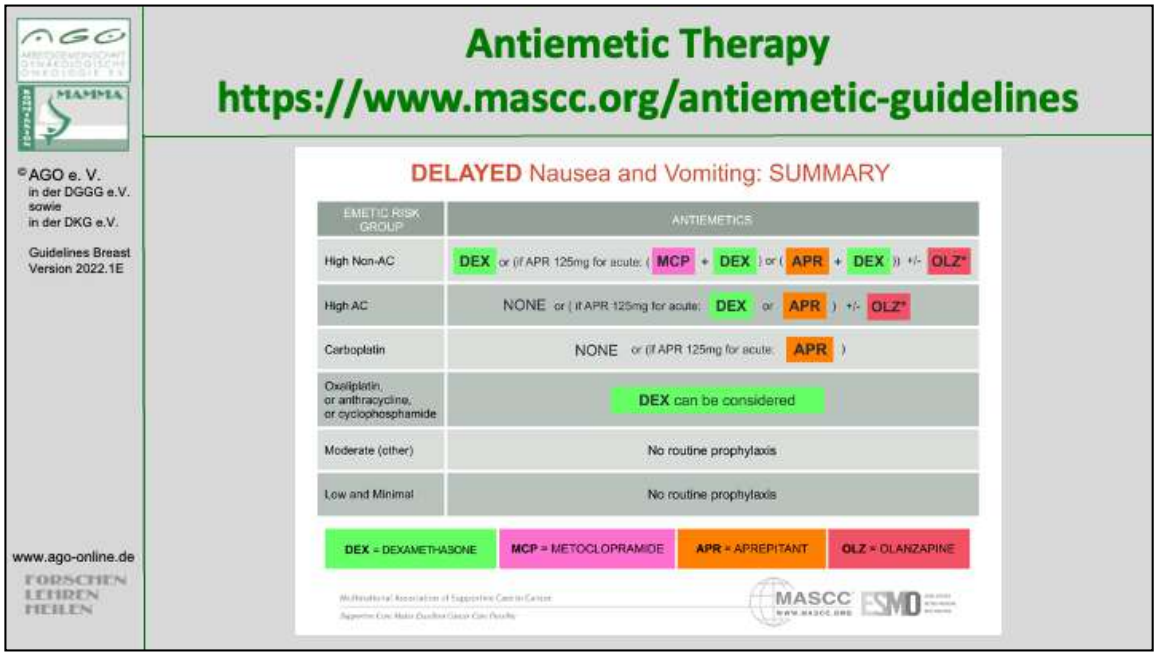

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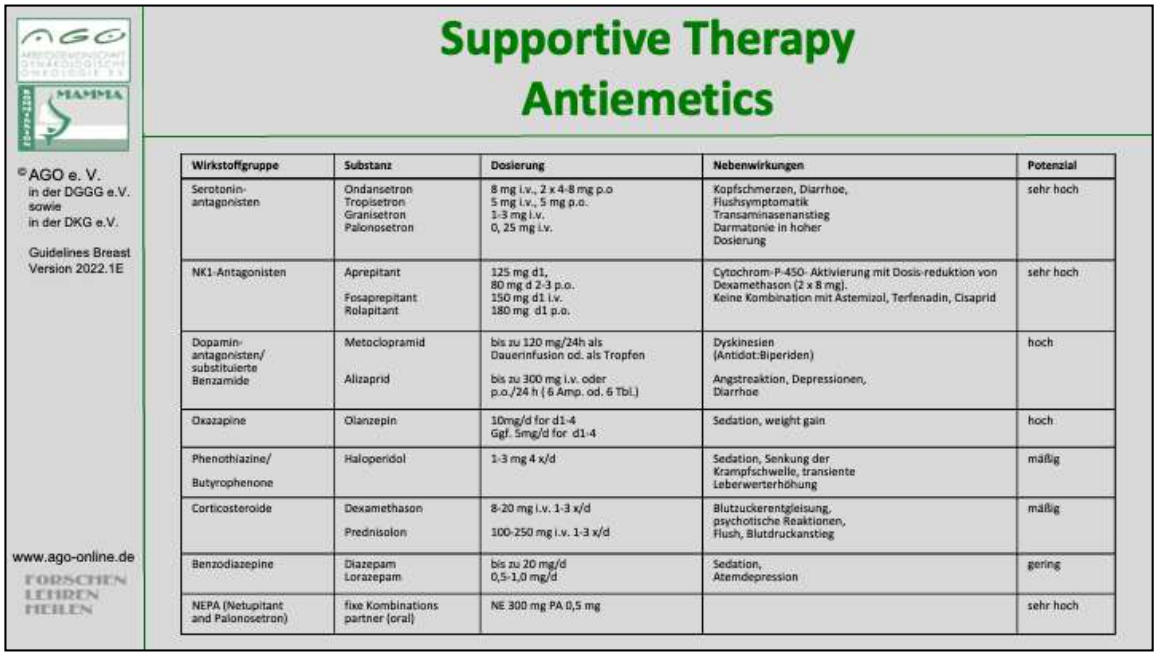

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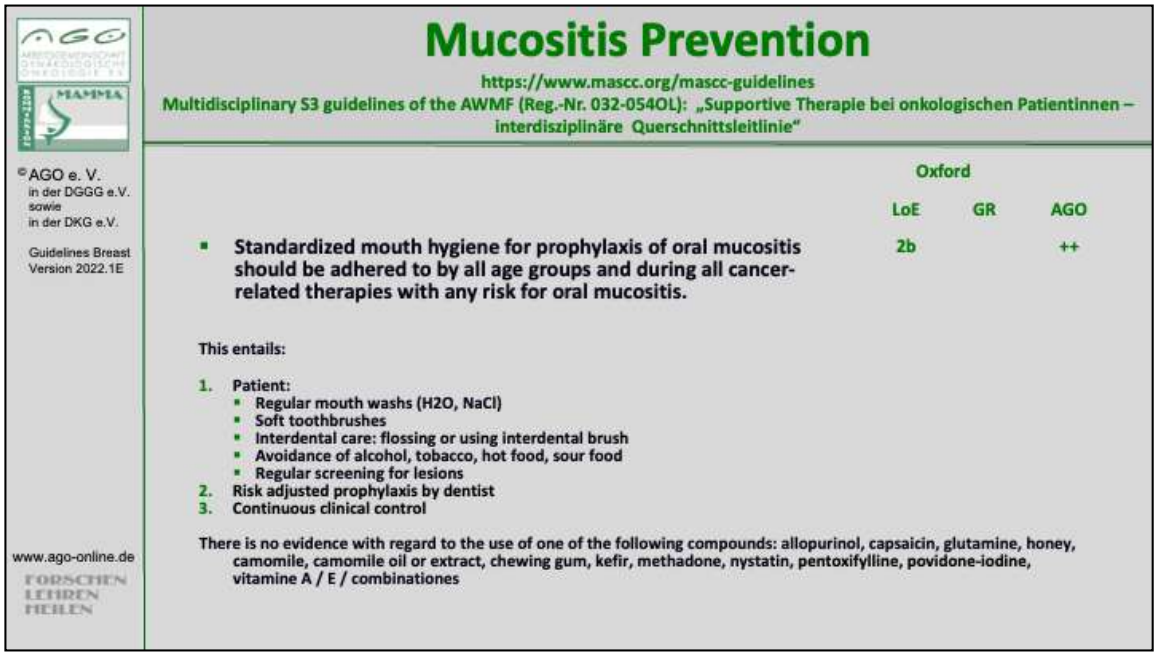

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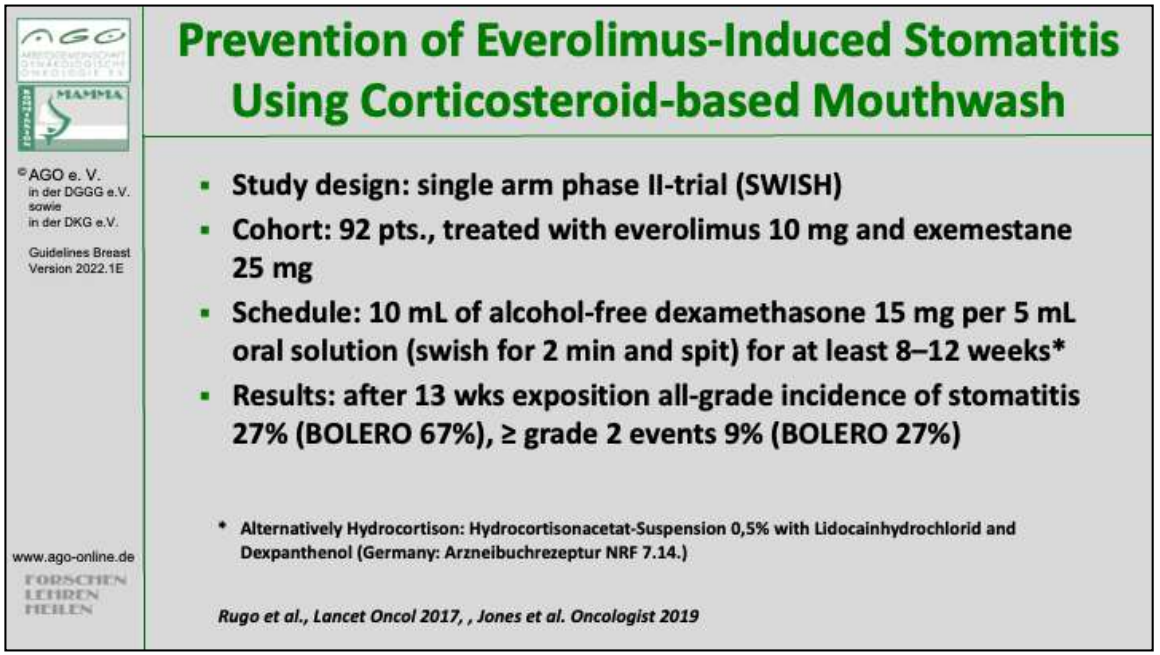

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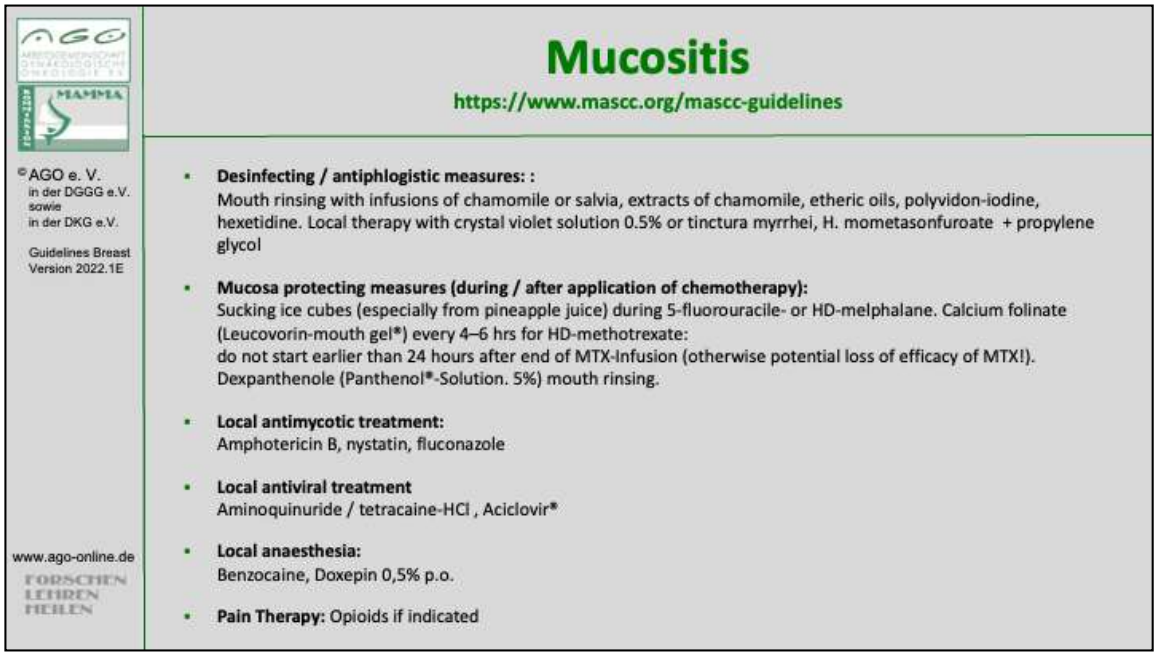

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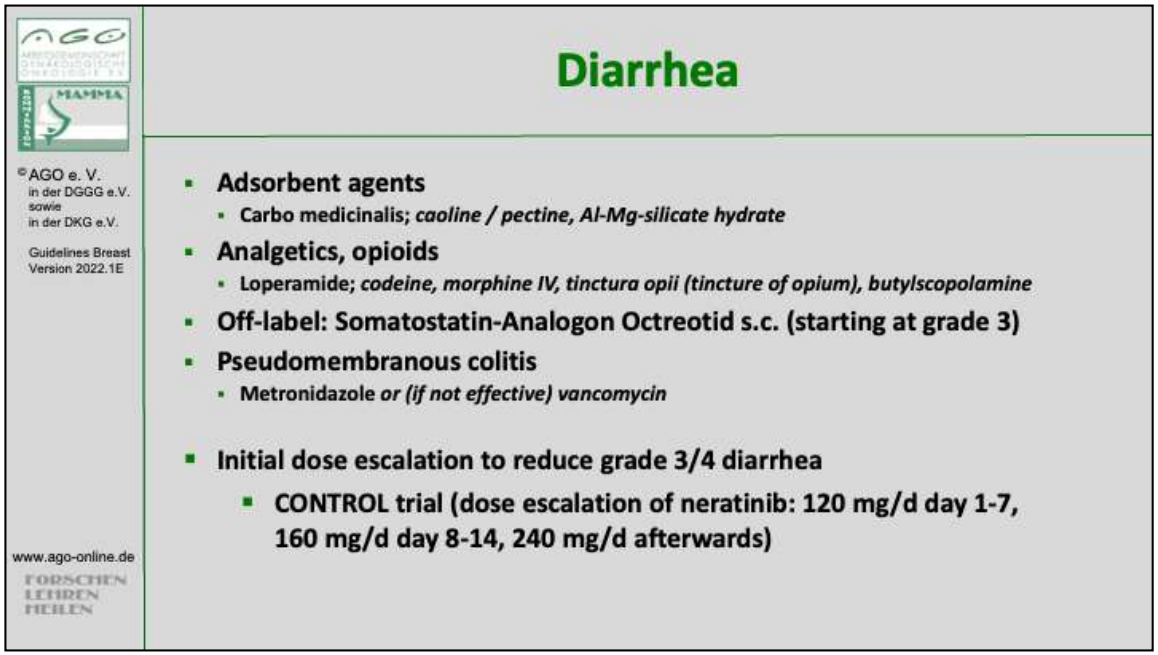

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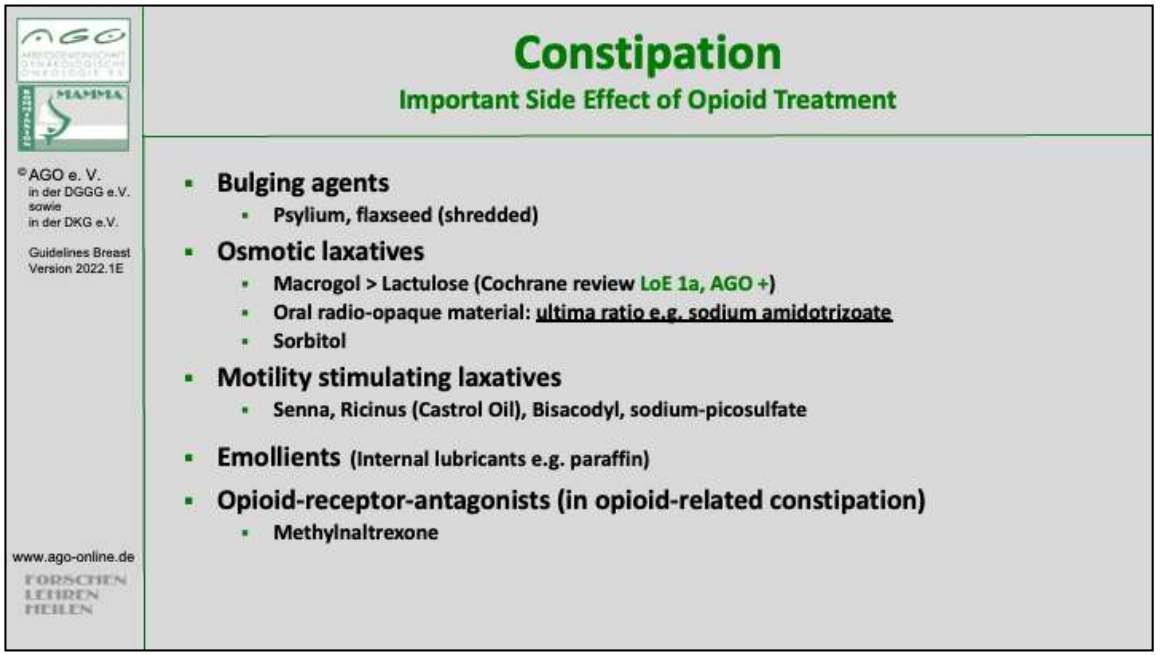

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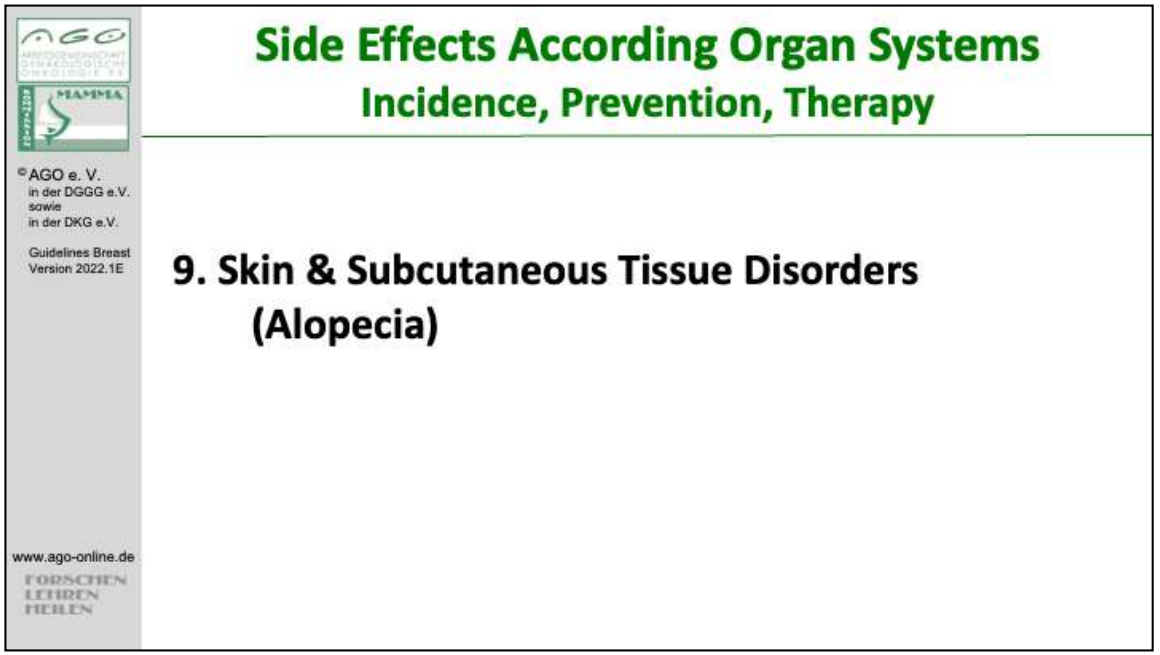

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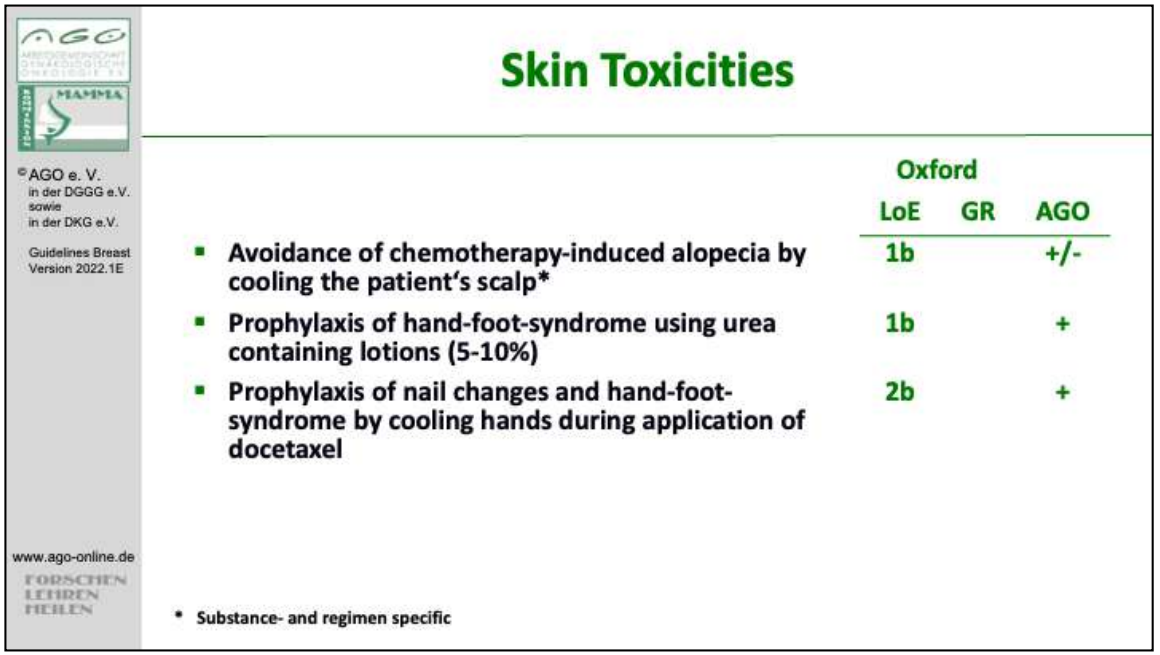

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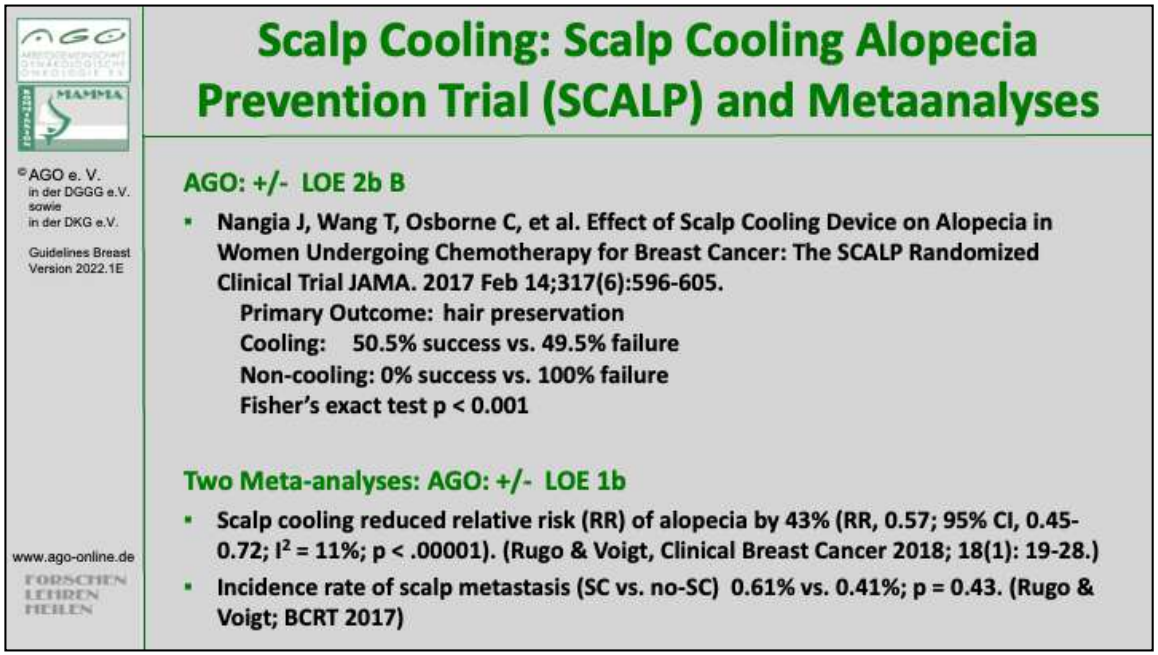

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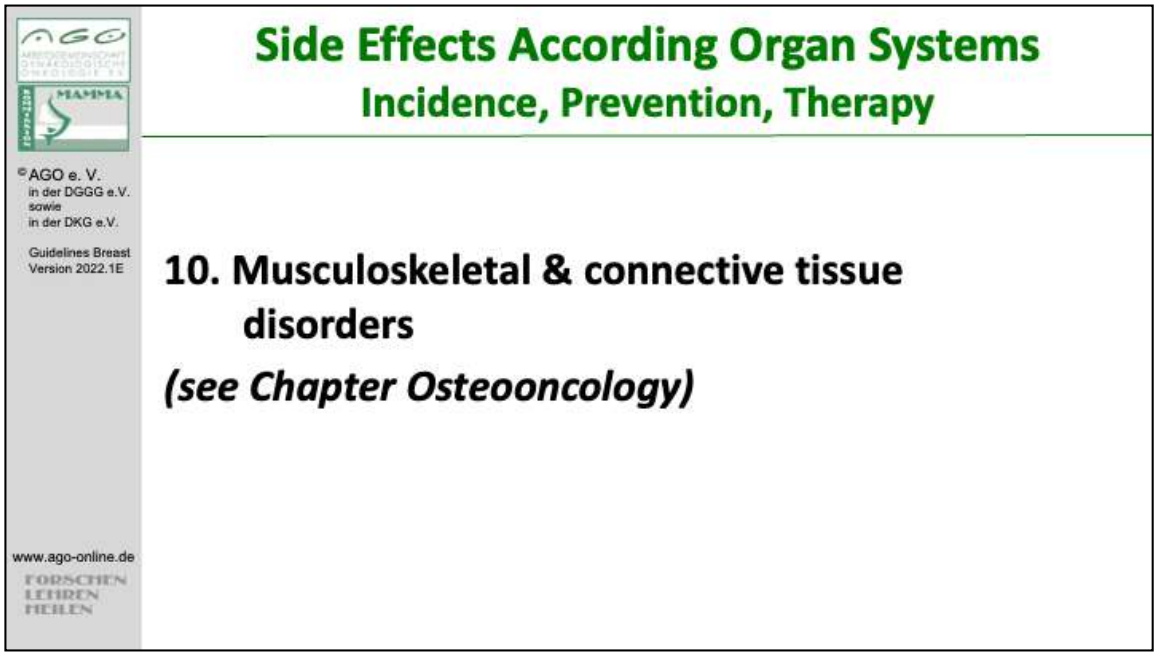

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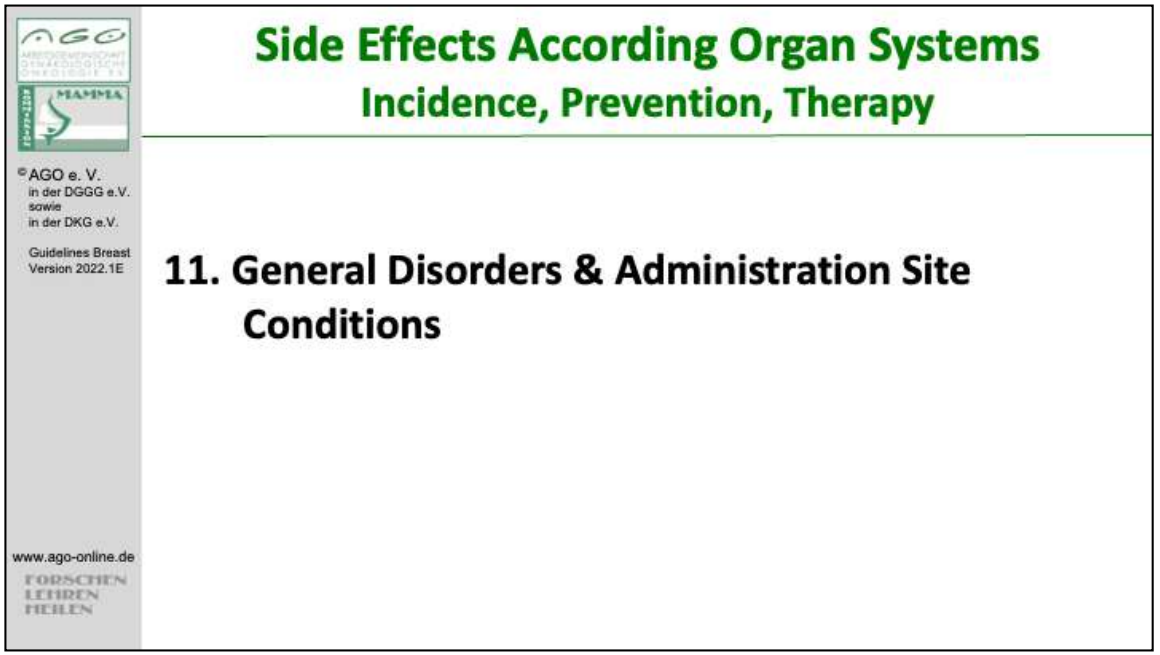

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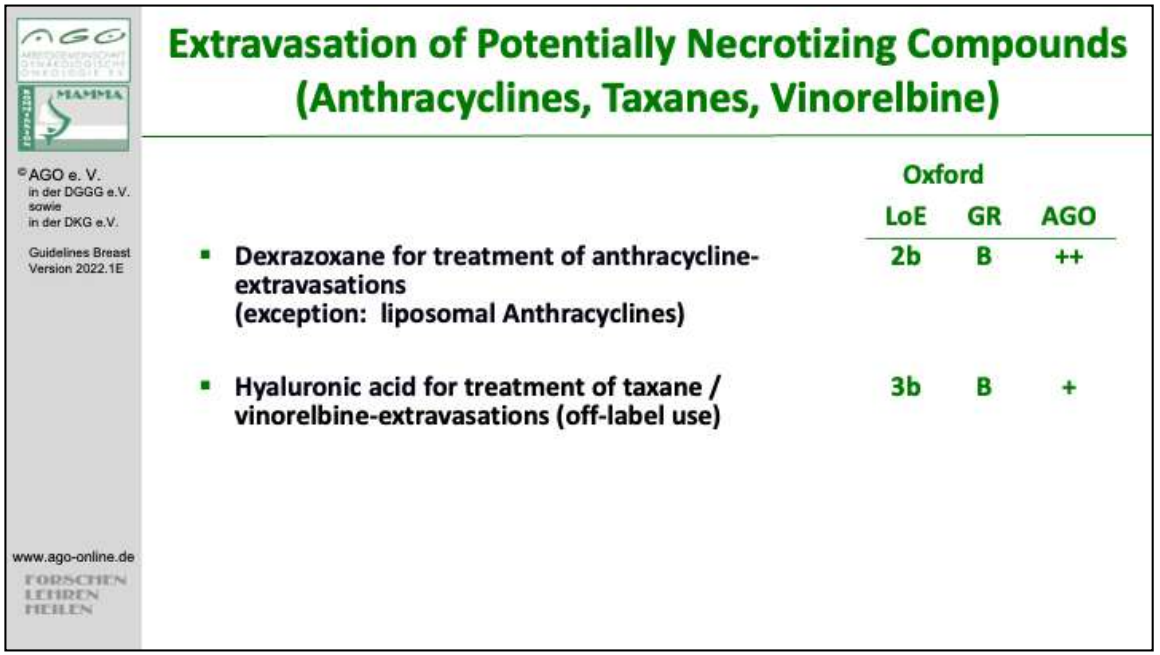

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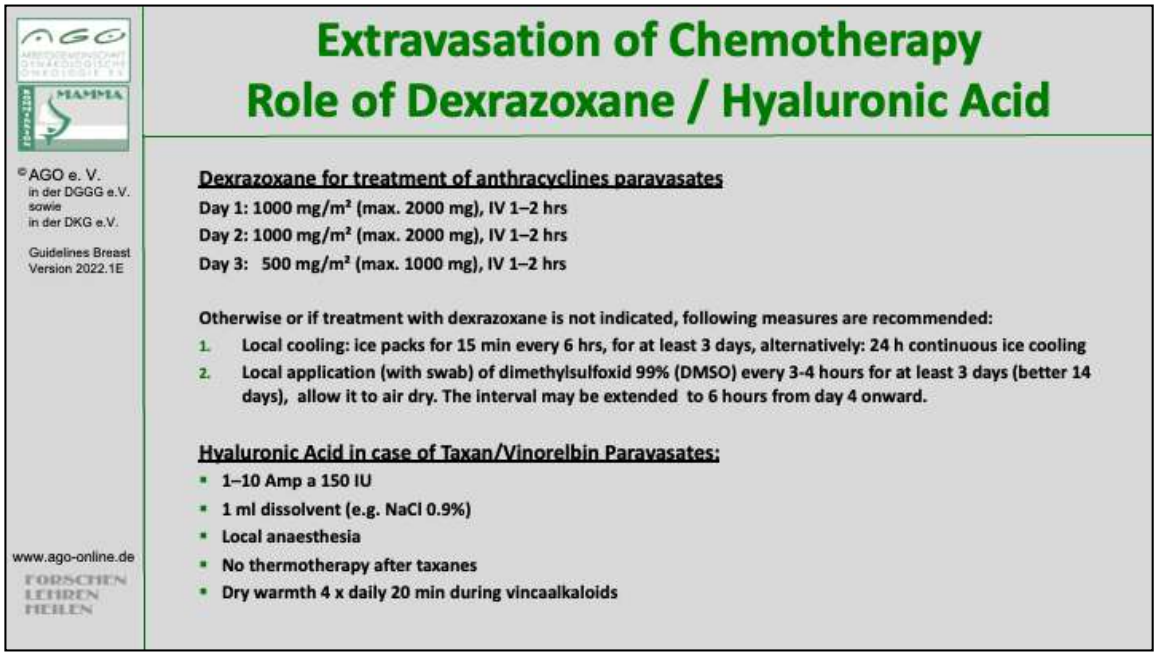

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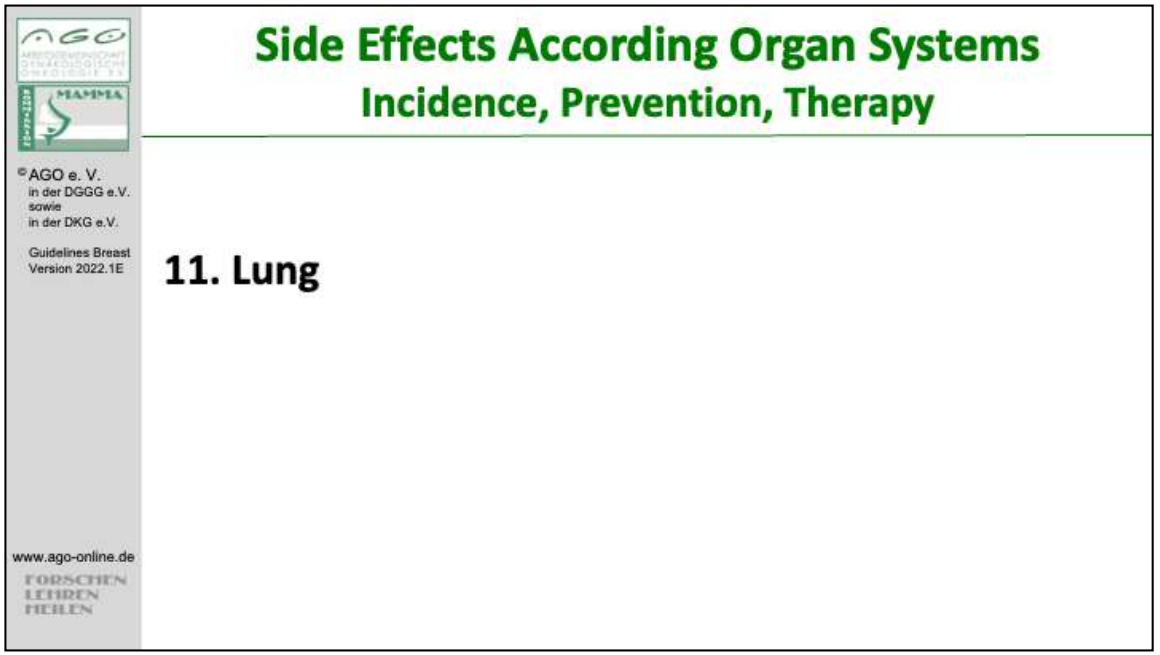

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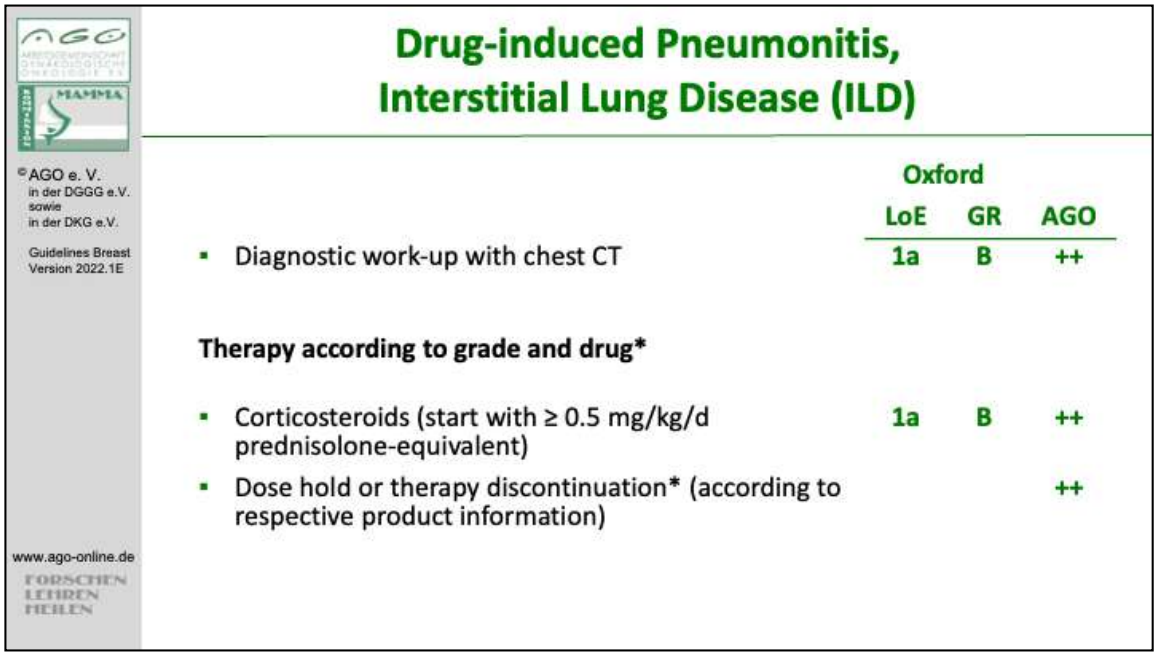

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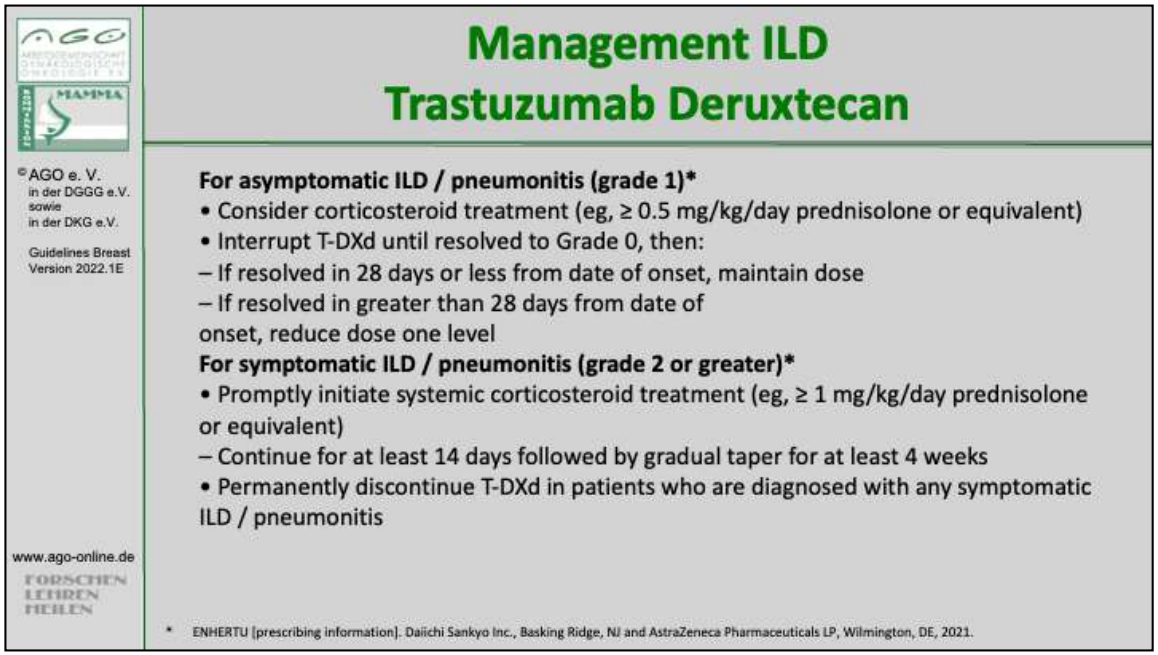

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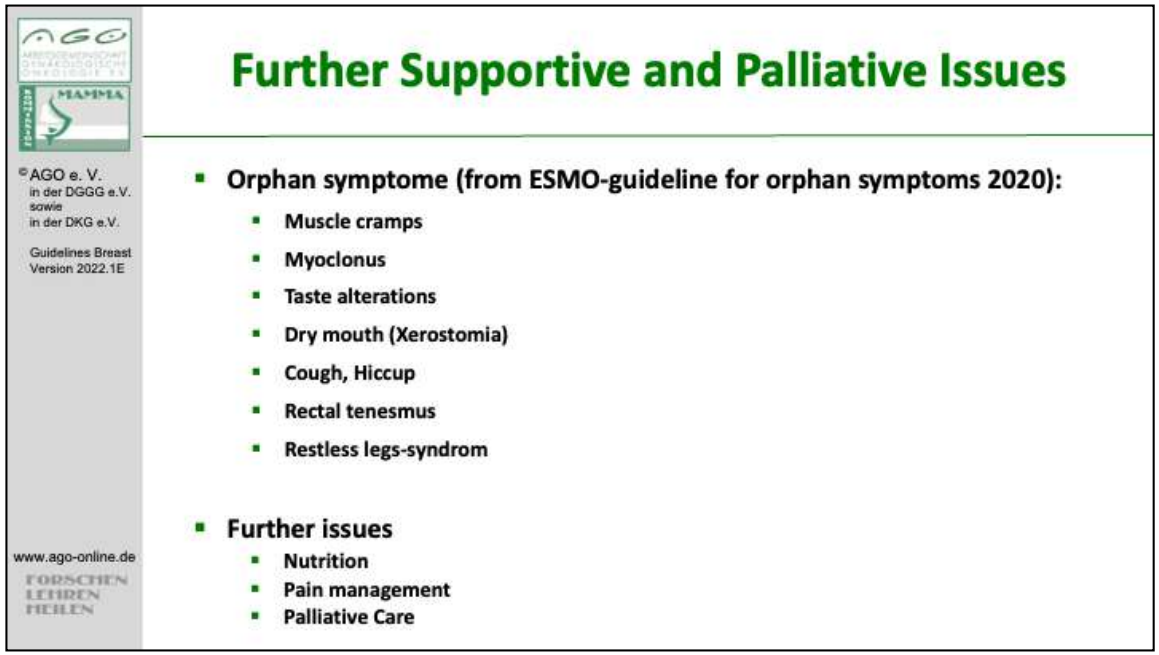

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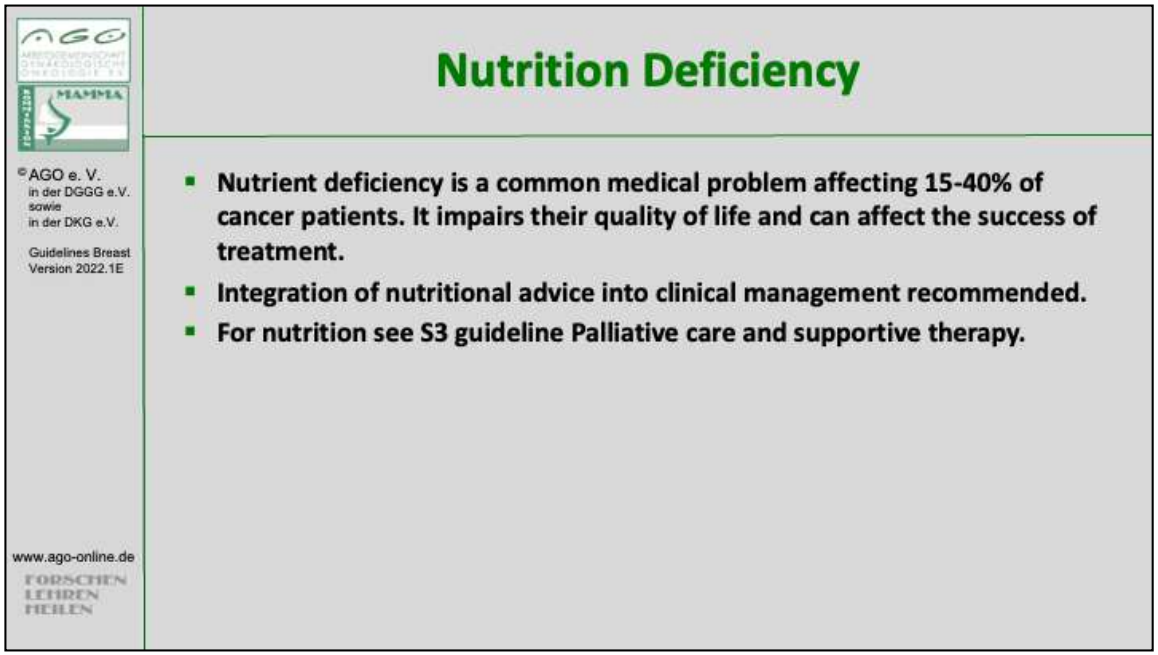

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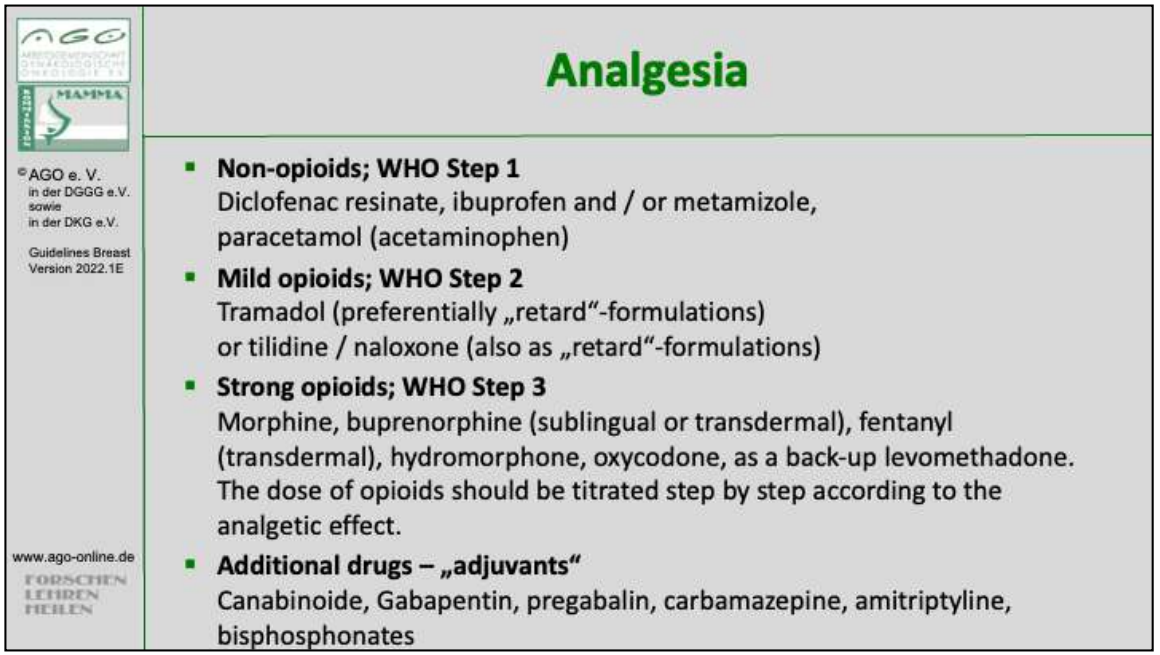

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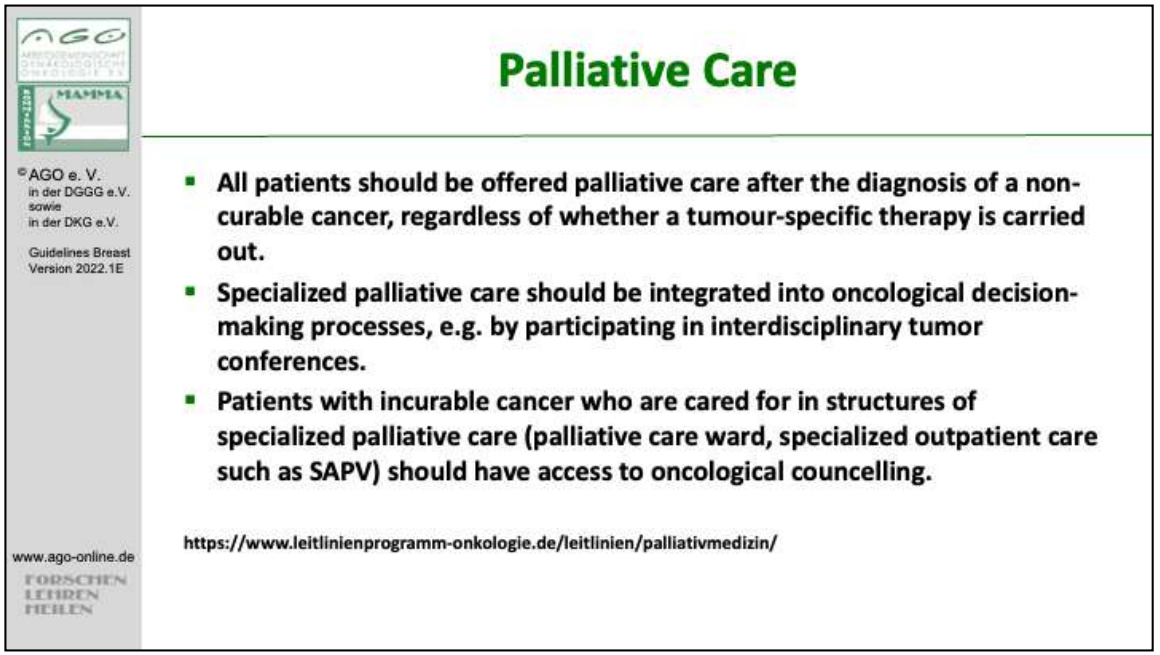

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