Screened data bases

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

Screened guidelines

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4. American Society of Clinical Oncology Clinical Practice Survivorship Guidelines, Endorsements and Adaptations: https://www.asco.org/practice-policy/cancer-care-initiatives/prevention-survivorship/survivorship-compendium-0
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7. NCCN (National Comprehensive Cancer Network , 2019): http://www.nccn.org
8. S3-Leitlinie: Supportive Therapie:
   Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.2 – November 2019 AWMF-Registernummer: 032/054OL Zugrifff 26.12.2019

Supportive Care and Management of Side Effects

Guidelines Breast
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- **Versionen 2002–2019:**
  Albert / Bauerfeind / Brunnert / Bischoff / Costa / Dall / Diel / Fersis / Friedrich / Friedrichs / Gerber / Göhring / Hanf / Harbeck / Heinrich / Huober / Jackisch / Lisboa / Lück / Lüftner / von Minckwitz / Möbus /Müller / Nitz / Oberhoff / Rody / Schaller / Scharl / Schmidt / Schneeweiss / Schütz / Solomayer / Souchon / Stickeler / Thomssen / Untch
- **Version 2020:**
  Müller / Albert

Content

- Guidelines
- Assessment of toxicity
- Incidence of side effects (according technical product information; MedDRA-standard)
- Side effects according organ systems
  - Incidence, prevention, therapy
- Substance specific side effects
  - Targeted drugs
- Further issues
  - Pain management, palliative care

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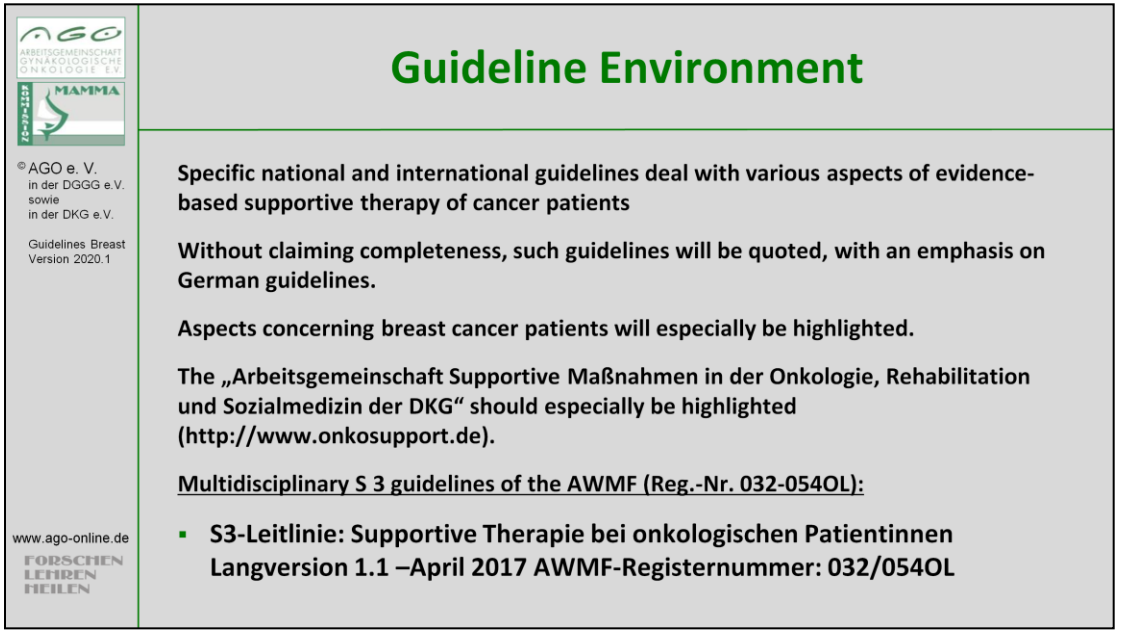
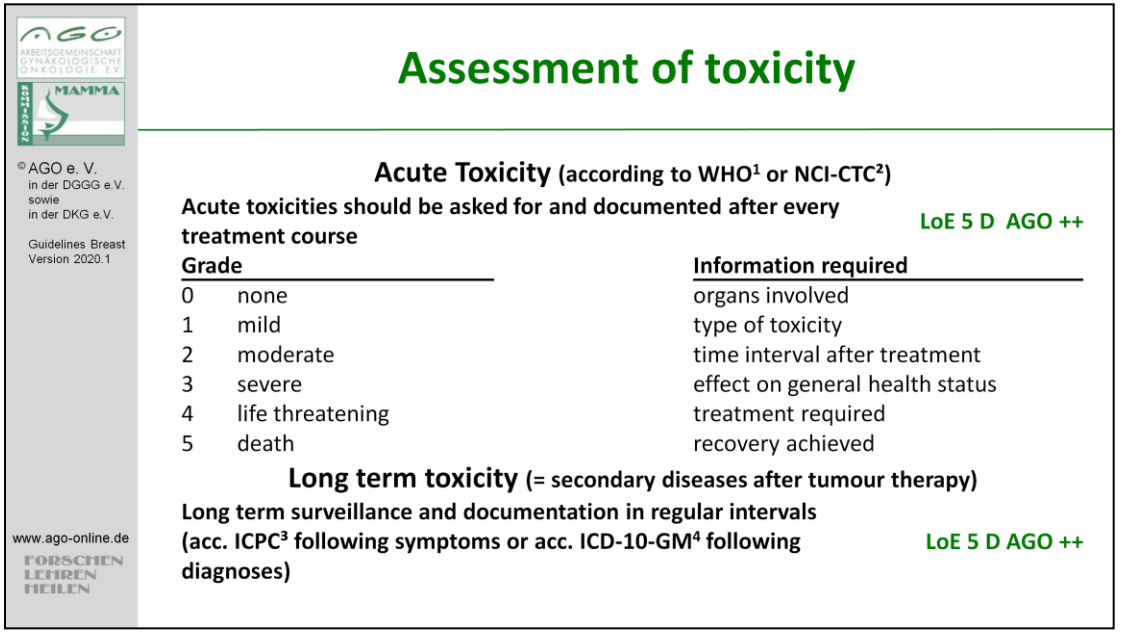
- **Guideline - environment**



1. S3-Leitlinie: Supportive Therapie:
   Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.2 – November 2019 AWMF-Registernummer: 032/054OL Zugrifff 26.12.2019

https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Supportivtherapie/LL_Supportiv_Langversion_1.2.pdf

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



Akute Toxizität

1. WHO Handbook for reporting results of cancer treatment, N0 48 (1979) (WHO offset Publications, Geneva)
2. 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)

Akute Toxizität nach jedem Therapiezyklus abfragen

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Langzeittoxizität

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)
2. Deutschen Institut für Medizinische Dokumentation und Information (DIMDI), ICD-10-GM Version 2017; https://www.dimdi.de/static/de/klassi/icd-10-gm/kodesuche/onlinefassungen/htmlgm2017/ (Download 18.01.2018)

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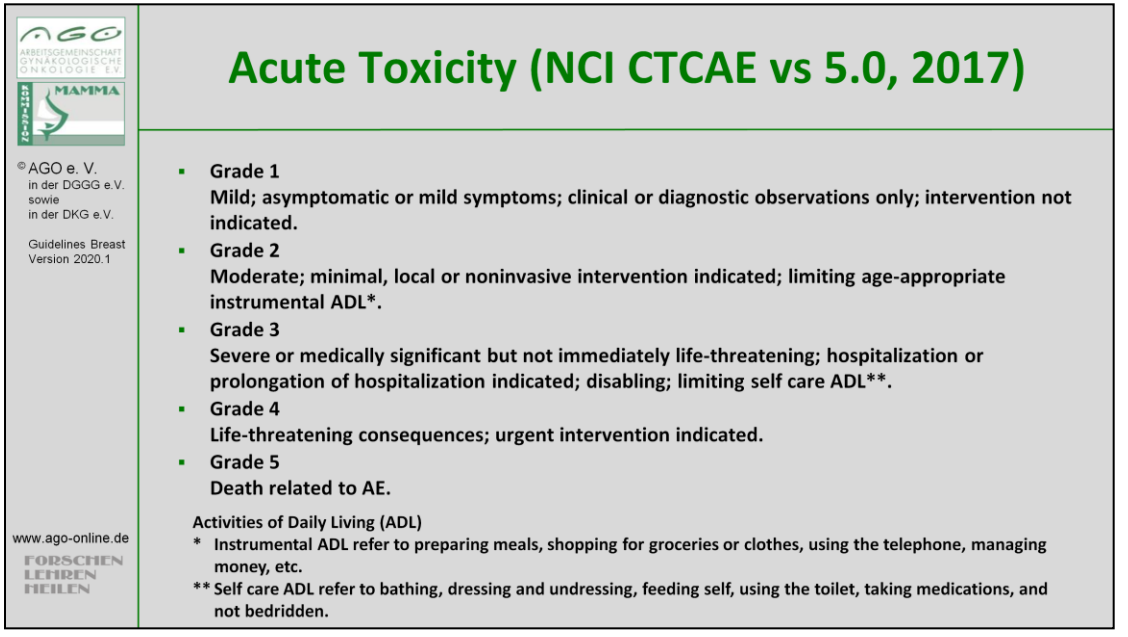
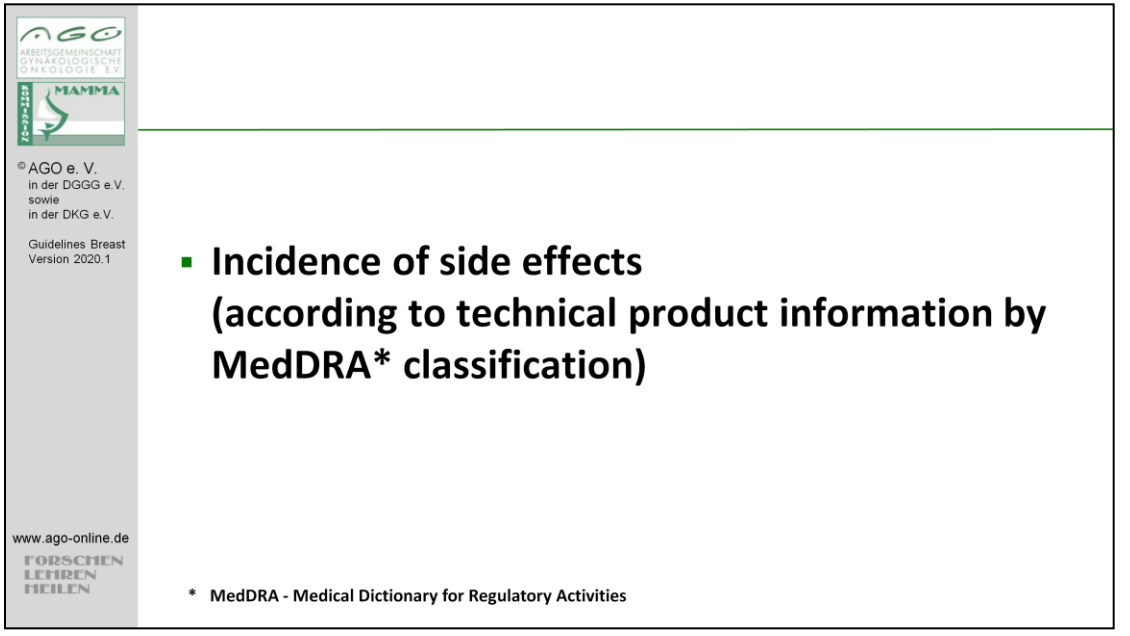
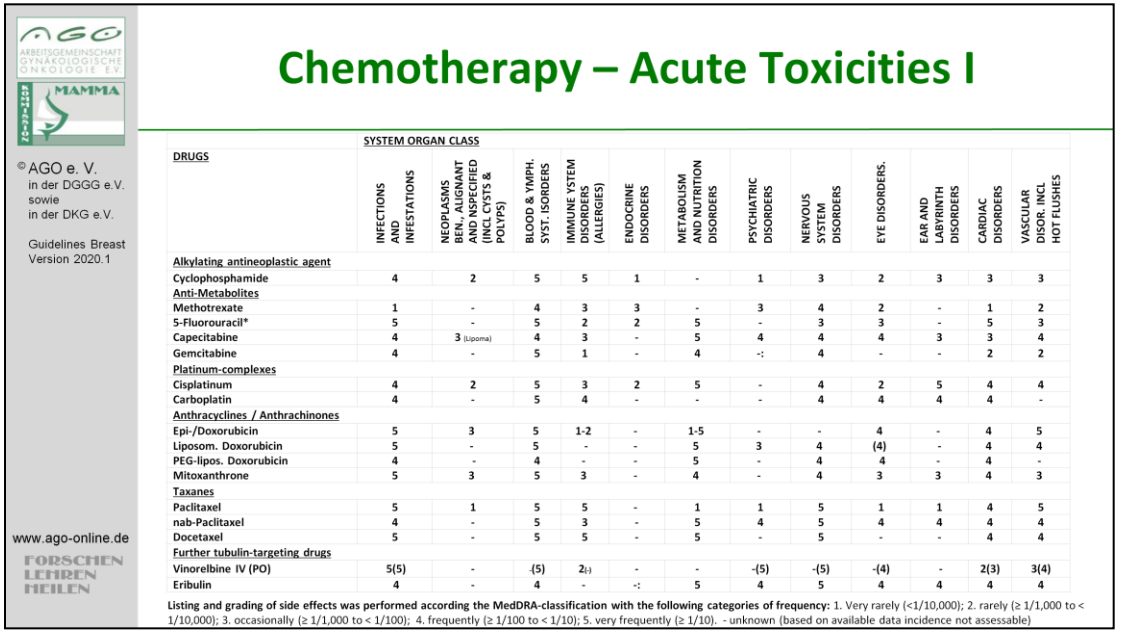


1. NCI, Bethesda, USA, Common Terminology Criteria for Adverse Events v5.0 (CTCAE; published 2017); https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50 (Download 18.01.2018)



*MedDRA - Medical Dictionary for Regulatory Activities

https://www.meddra.org/



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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)

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

Epirubicin:
Doxorubicin:
Liposomales Doxorubicin: https://www.gelbe-liste.de/produkte/Myocet-50-mg-Pulver-Dispersion-u-Loesungsmittel-fuer-ein-Konzentrat-zur-Herstellung-einer-Infusionsdispersion_359323/fachinformation
PEG-lipo. Doxorubicin: https://www.gelbe-liste.de/produkte/Caelyx-2-mg-ml-Konzentrat-zur-Herstellung-einer-Infusionsloesung-10-ml_121890/fachinformation
Mitoxantron: https://www.gelbe-liste.de/produkte/Mitoxantron-Teva-2-mg-ml-Injektionsloesung-15ml_543783/fachinformation
Paclitaxel: https://medikamio.com/de-de/medikamente/paclitaxel-ratiopharm/pil
Nab-Paclitaxel: https://www.gelbe-liste.de/produkte/Abraxane-5-mg-ml-Pulver-zur-Herstellung-einer-Infusionssuspension_514889/fachinformation
Docetaxel: https://mein.sanofi.de/produkte/Taxotere/Downloads?id=89447754-dfb2-450b-b35a-36950de8a74d
Vinorelbin: http://www.detect-studien.de/dokumente/d3/fachinfo/Navelbine.pdf
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
4. Cortes J, O'Shaughnessy J, Loesch D et al. Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study. Lancet. 2011;377:914-23
5. Link, H. and S. Schmitz (2013). "Treatment of cancer-associated anaemia: results from a two-day cross-sectional survey in Germany." Onkologie 36(5): 266-272.
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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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.
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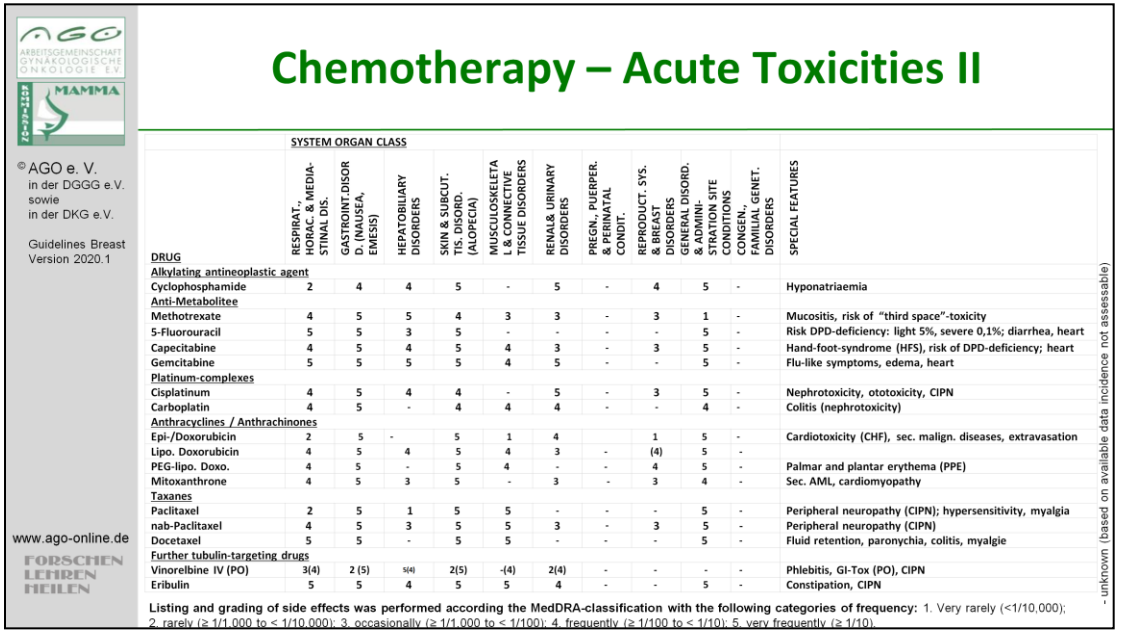
12. Madeddu C, Deidda M, Piras A, et al. Pathophysiology of cardiotoxicity induced by nonanthracycline chemotherapy. J Cardiovasc Med (Hagerstown). 2016 May;17 Suppl 1 Special issue on Cardiotoxicity from Antiblastic Drugs and Cardioprotection:e12-e18. Review.



Chemotherapy – Acute Toxicities II

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	SYSTEM ORGAN CLASS										
DRUG	RESPIRAT., HORAC. & MEDIASTINAL DIS.	GASTROINT.DISORD. (NAUSEA, EMESIS)	HEPATOBILIARY DISORDERS	SKIN & SUBCUT. TIS. DISORD. (ALOPECIA)	MUSCULOSKELETAL & CONNECTIVE TISSUE DISORDERS	RENAL& URINARY DISORDERS	PREGN., PUERPER. & PERINATAL CONDIT.	REPRODUCT. SYS. & BREAST DISORDERS	GENERAL DISORD. & ADMINISTRATION SITE CONDITIONS	CONGEN., FAMILIAL GENET. DISORDERS	SPECIAL FEATURES
Alkylating antineoplastic agent											
Cyclophosphamide	2	4	4	5	-	5	-	4	5	-	Hyponatriaemia
Anti-Metabolitee											
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, myalgie
Further tubulin-targeting drugs											
Vinorelbine 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	-	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).

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)

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)

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

Gemcitabin: http://www.success-studie.de/b/downloads/Fachinfo/GemzarFI07Jan.pdf
Cisplatin: https://www.gelbe-liste.de/produkte/Cisplatin-Teva-1-mg-ml-Konzentrat-zur-Herstellung-einer-Infusionsloesung-100-ml_543960/fachinformation
Carboplatin: http://www.teva.de/index.php?eID=dumpFile&t=f&f=37532&g=-1&r=11068%2C11068&token=eebfb22e78f1cc8d9935d59c087e80630146f49e
Epirubicin:
Doxorubicin:
Liposomales Doxorubicin: https://www.gelbe-liste.de/produkte/Myocet-50-mg-Pulver-Dispersion-u-Loesungsmittel-fuer-ein-Konzentrat-zur-Herstellung-einer-Infusionsdispersion_359323/fachinformation
PEG-lipo. Doxorubicin: https://www.gelbe-liste.de/produkte/Caelyx-2-mg-ml-Konzentrat-zur-Herstellung-einer-Infusionsloesung-10-ml_121890/fachinformation
Mitoxantron: https://www.gelbe-liste.de/produkte/Mitoxantron-Teva-2-mg-ml-Injektionsloesung-15ml_543783/fachinformation
Paclitaxel: https://medikamio.com/de-de/medikamente/paclitaxel-ratiopharm/pil
Nab-Paclitaxel: https://www.gelbe-liste.de/produkte/Abraxane-5-mg-ml-Pulver-zur-Herstellung-einer-Infusionssuspension_514889/fachinformation
Docetaxel: https://mein.sanofi.de/produkte/Taxotere/Downloads?id=89447754-dfb2-450b-b35a-36950de8a74d
Vinorelbin: http://www.detect-studien.de/dokumente/d3/fachinfo/Navelbine.pdf
Eribulin: http://www.detect-studien.de/dokumente/d4/fachinfo/Fachinfo_Eribulin_Halaven.pdf

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breast cancer (EMBRACE): a phase 3 open-label randomised study. Lancet. 2011;377:914-23
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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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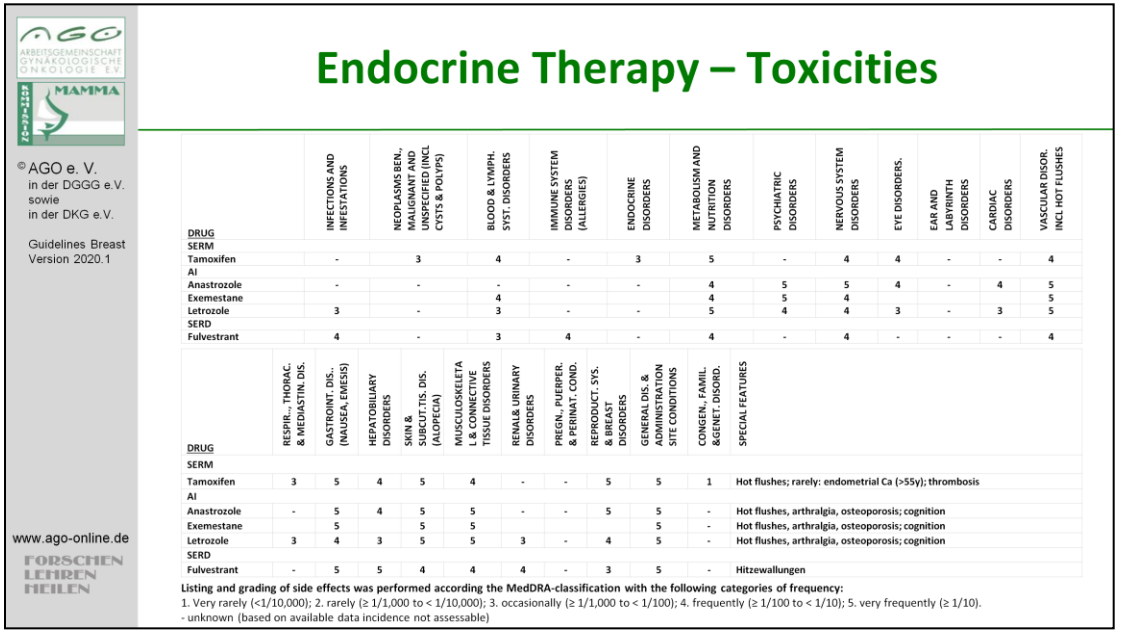

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DRUG	INFECTIONS AND INFESTATIONS	NEOPLASMS BEN., MALIGNANT AND UNSPECIFIED (INCL CYSTS & POLYPS)	BLOOD & LYMPH. SYST. DISORDERS	IMMUNE SYSTEM DISORDERS (ALLERGIES)	ENDOCRINE DISORDERS	METABOLISM AND NUTRITION DISORDERS	PSYCHIATRIC DISORDERS	NERVOUS 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)	MUSCULOSKELETAL & CONNECTIVE TISSUE DISORDERS	RENAL& URINARY DISORDERS	PREGN., PUERPER. & PERINAT. COND.	REPRODUCT. SYS. & BREAST DISORDERS	GENERAL DIS. & ADMINISTRATION 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)

Nebenwirkungskategorien - MedDRA (Medical Dictionary for Regulatory Activities)
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)
Tamoxifen: https://www.gelbe-liste.de/produkte/Tamoxifen-20-mg-HEXAL-Filmtbl_8660/fachinformation

Anastrozol: https://imedikament.de/anastrozol-ratiopharm-1-mg-filmtabletten/fachinformation
Exemestan: http://www.success-studie.de/c/downloads/Fachinfo/FI_ExemestanAromasin.pdf
Letrozol: http://www.success-studie.de/b/downloads/Fachinfo/Femara_Juli_2014.pdf

Fulvestrant: https://www.gelbe-liste.de/produkte/Fulvestrant-HEXAL-250-mg-Injektionsloesung-in-einer-Fertigspritze_912622/fachinformation

Guidelines Breast
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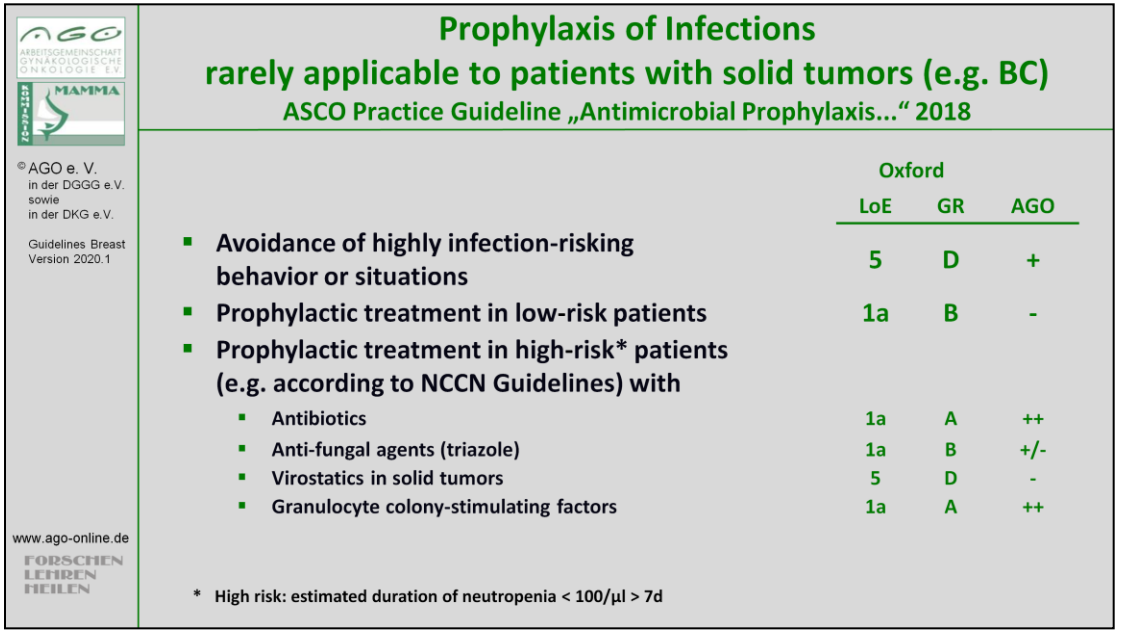
Side effects according Organ Systems
Incidence, Prevention, Therapy

1. **Infections and infestations**
   - **General prophylaxis for infections**
   - **Hepatitis B virus screening**

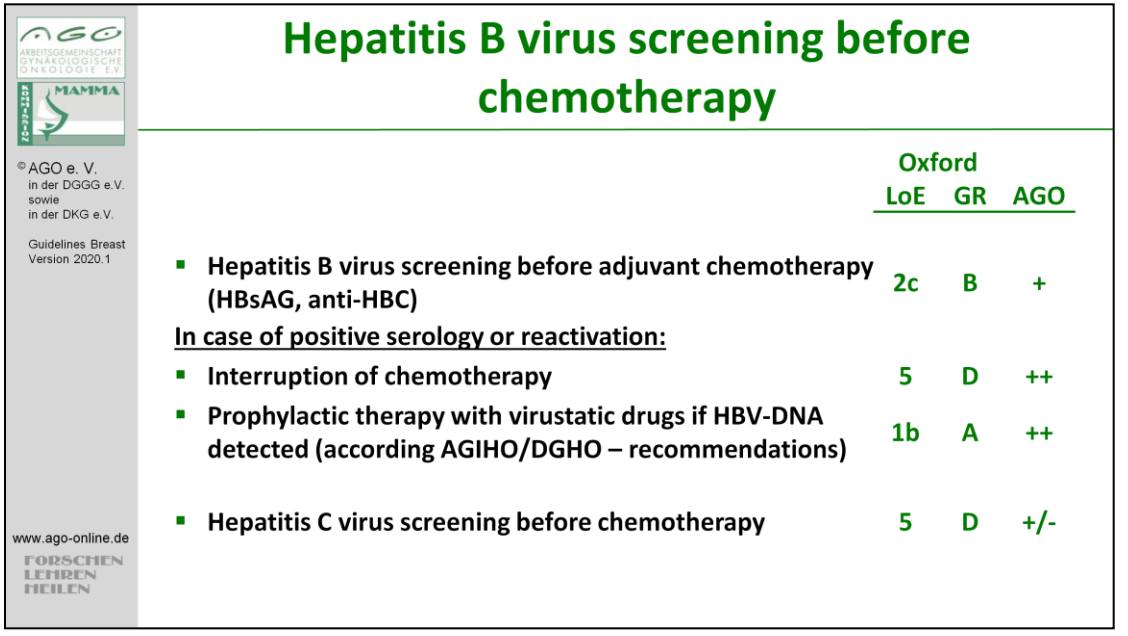


ASCO:

Taplitz RA, Kennedy EB, Bow EJ, Crews J, Gleason C, Hawley DK, Langston AA, Nastoupil LJ, Rajotte M, Rolston K, Strasfeld L, Flowers CR: Outpatient management of fever and neutropenia in adults treated for malignancy: American society of clinical oncology and infectious diseases society of america clinical practice guideline update. J Clin Oncol 2018;36:1443-1453.

NCCN:

NCCN Guidelines Version 1.2020 Prevention and Treatment of Cancer-Related Infections.
https://www.nccn.org/professionals/physician_gls/PDF/infections.pdf



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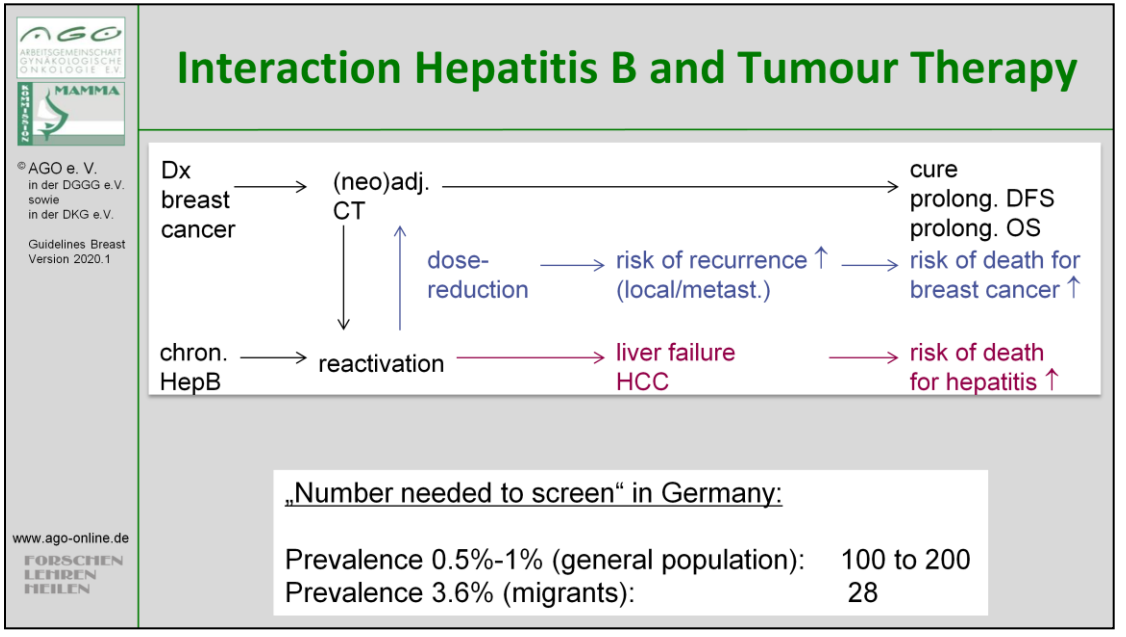

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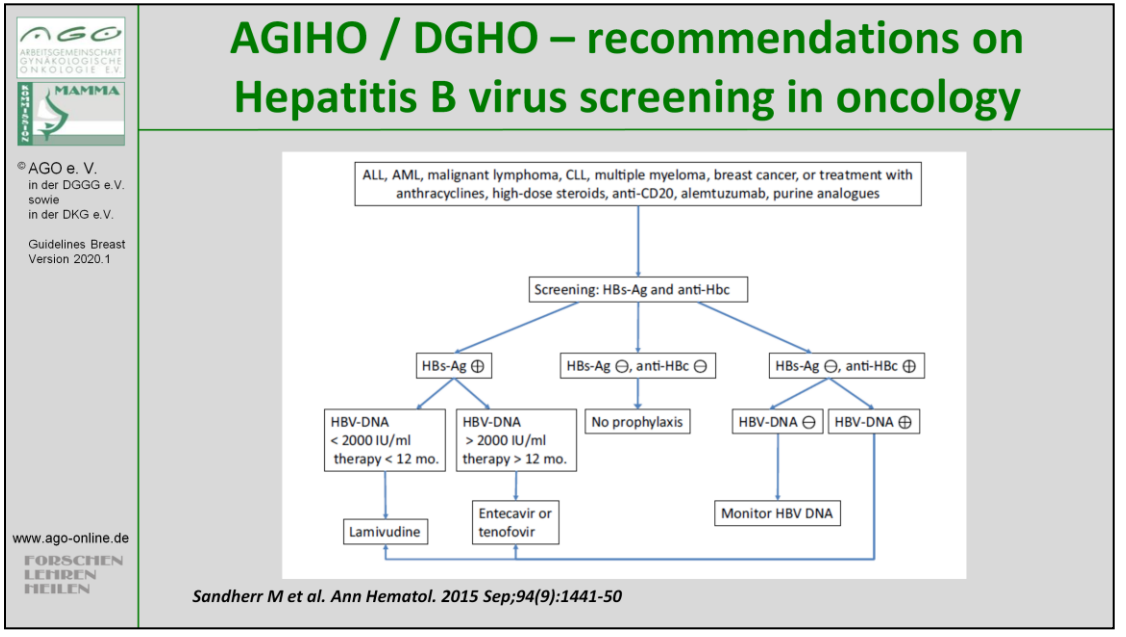

1. Sandherr M, Hentrich M, von Lilienfeld-Toal M, et al. Antiviral prophylaxis in patients with solid tumours and haematological malignancies--update of the Guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society for Hematology and Medical Oncology (DGHO). Ann Hematol. 2015 Sep;94(9):1441-50.
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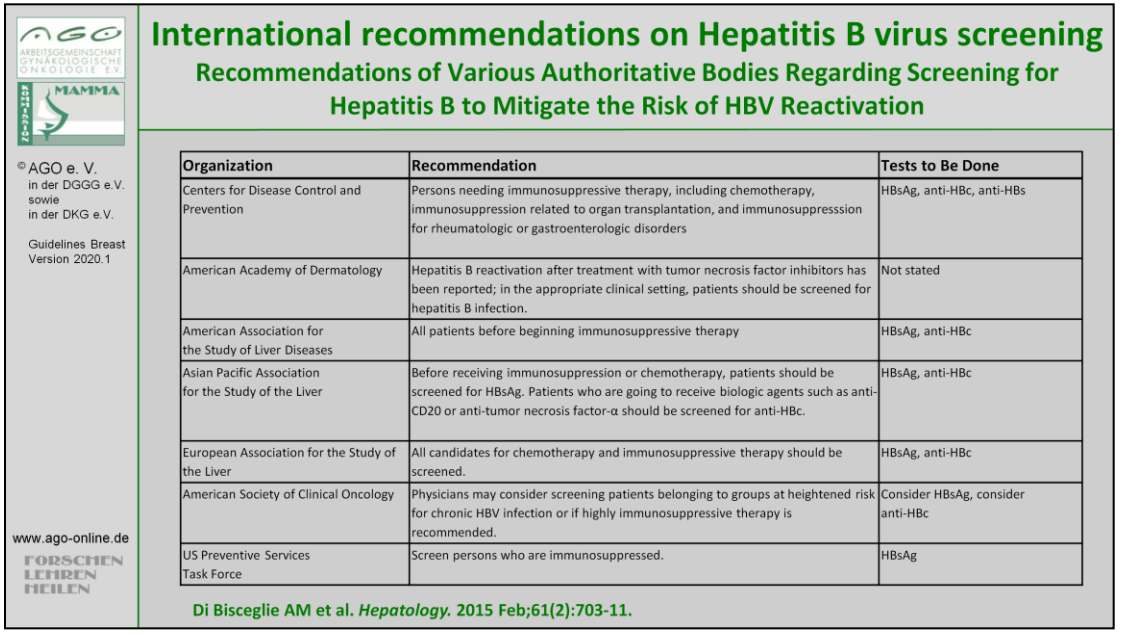

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Side Effects According Organ Systems
Incidence, Prevention, Therapy

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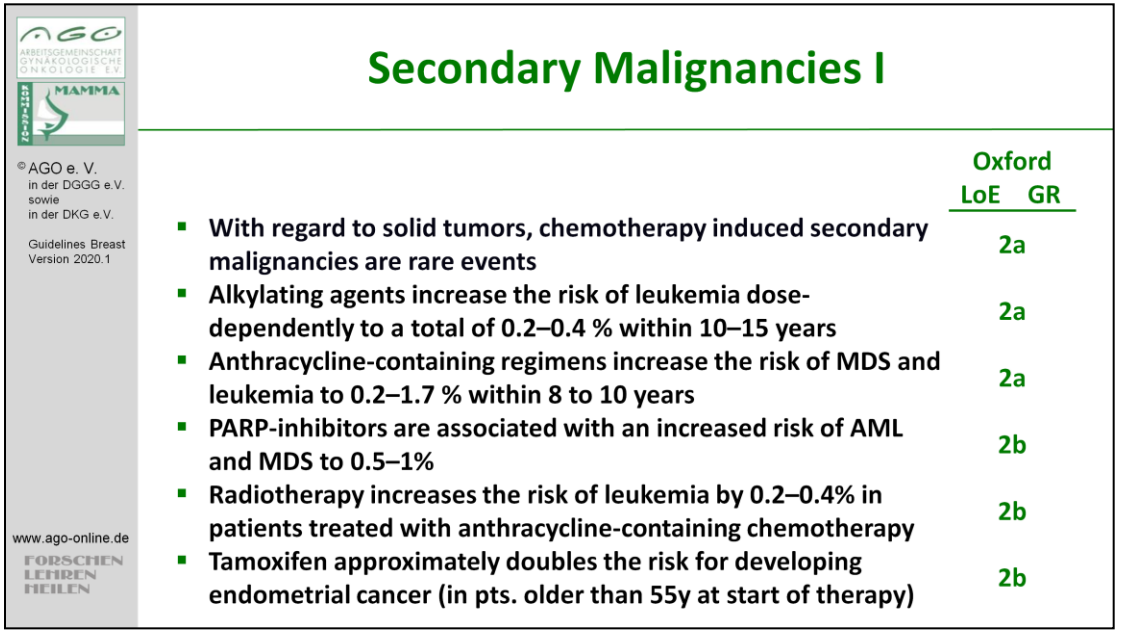
2. Neoplasms benign, malignant and unspecified (incl. cysts and polyps)



Statements 1-4

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Tamoxifen and endometrial cancer

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Davies C, Godwin J, et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet. 2011 Aug 27;378(9793):771-84.
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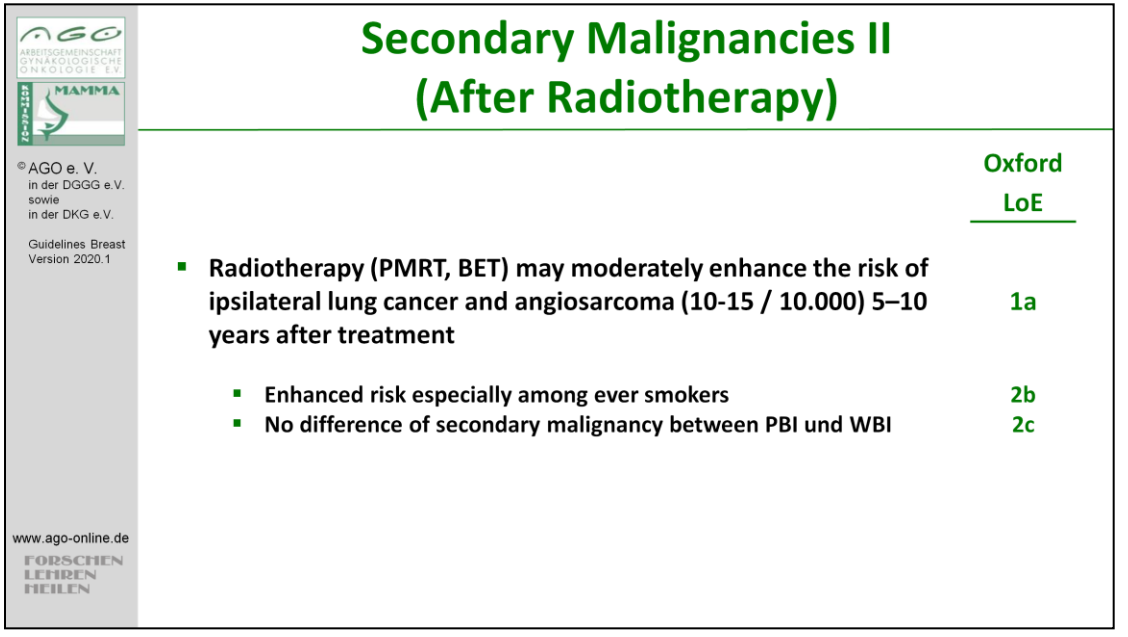

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10. Wei JL, Jiang YZ, Shao ZM: Survival and chemotherapy-related risk of second primary malignancy in breast cancer patients: A seer-based study. Int J Clin Oncol 2019;24:934-940.
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Guidelines Breast
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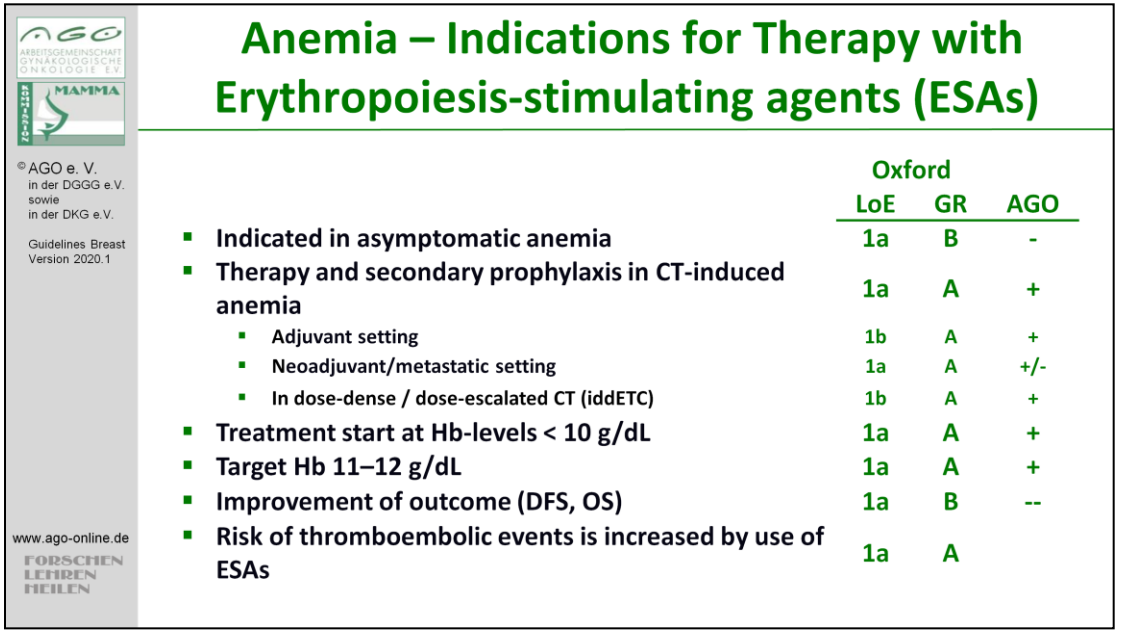
Side Effects According Organ Systems
Incidence, Prevention, Therapy

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 1.2, 2019,

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<u>Relevante Leitlinien</u>

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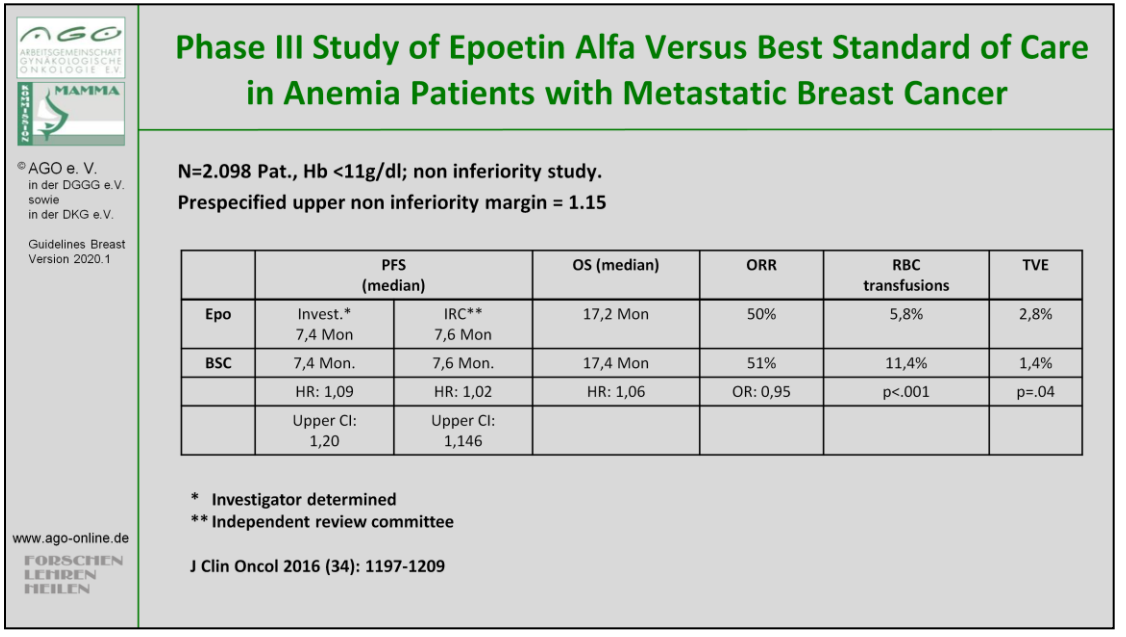


Phase III Study of Epoetin Alfa Versus Best Standard of Care in Anemia Patients with Metastatic Breast Cancer

N=2.098 Pat., Hb <11g/dl; non inferiority study.

Prespecified upper non inferiority margin = 1.15

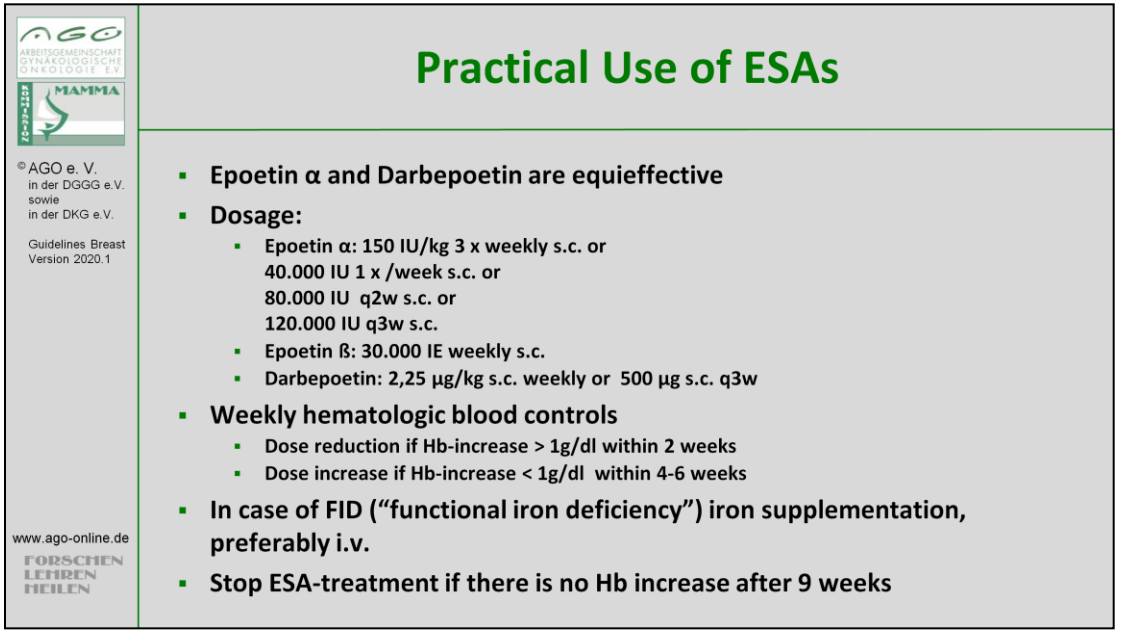
	PFS (median)		OS (median)	ORR	RBC transfusions	TVE
Epo	Invest.* 7,4 Mon	IRC** 7,6 Mon	17,2 Mon	50%	5,8%	2,8%
BSC	7,4 Mon.	7,6 Mon.	17,4 Mon	51%	11,4%	1,4%
	HR: 1,09	HR: 1,02	HR: 1,06	OR: 0,95	p<.001	p=.04
	Upper CI: 1,20	Upper CI: 1,146				

* **Investigator determined**

** **Independent review committee**

J Clin Oncol 2016 (34): 1197-1209

1. Leyland-Jones B, Bondarenko I et al. J Clin Oncol 2016 (34): 1197-1209



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<u>Relevante Leitlinien</u>

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Cancer- and Chemotherapy-Induced Anemia. Version 2.2018

(https://www.nccn.org/professionals/physician_gls/pdf/anemia.pdf)
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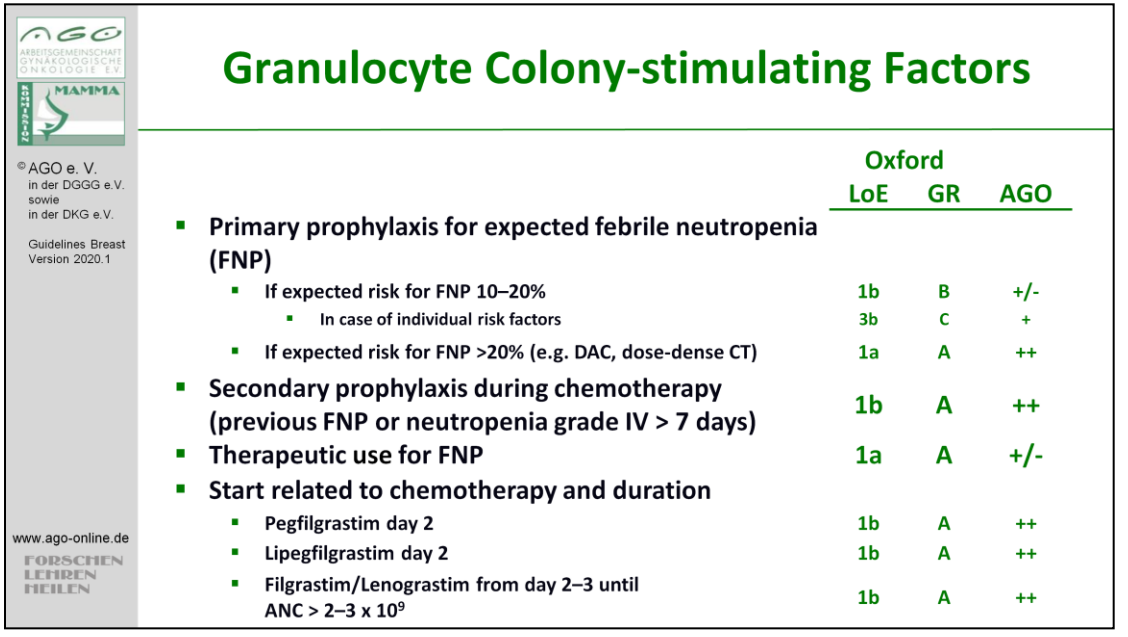

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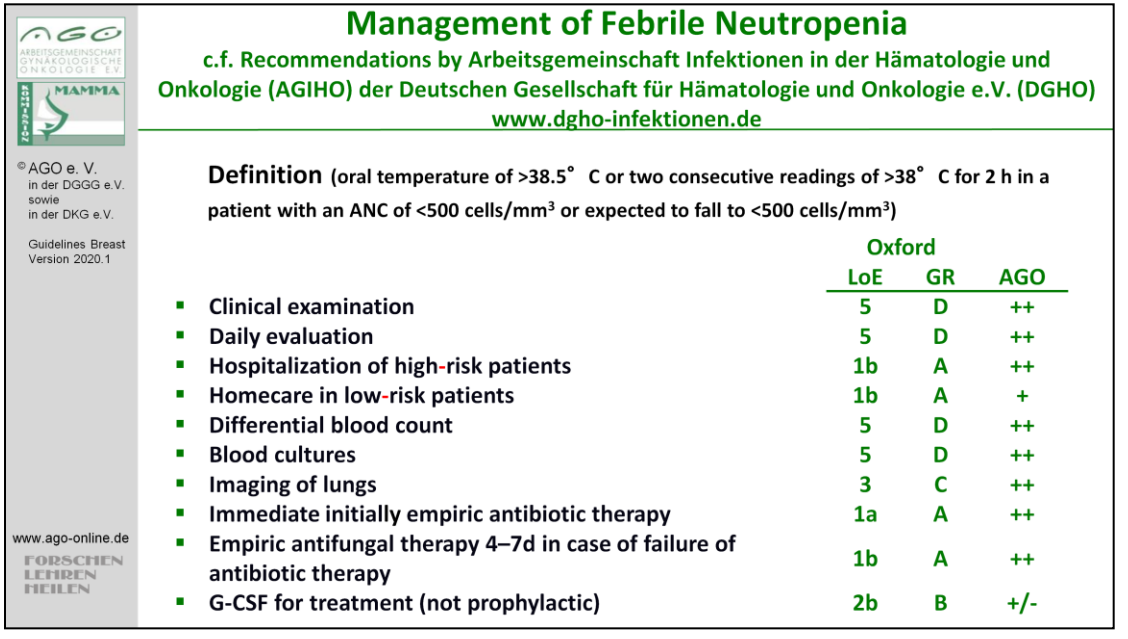

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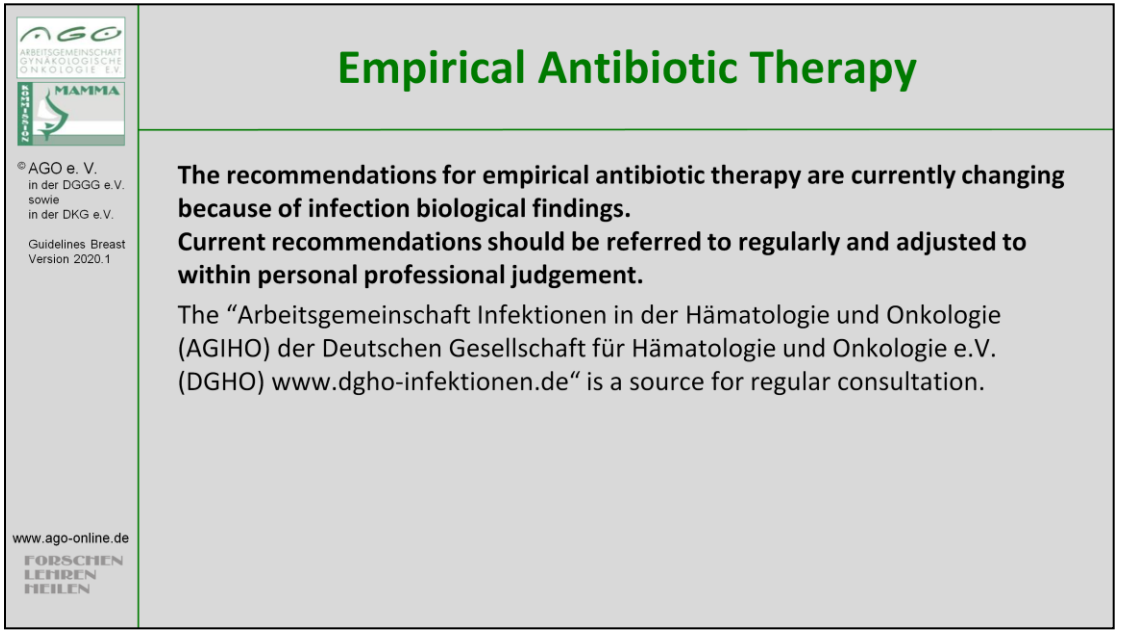

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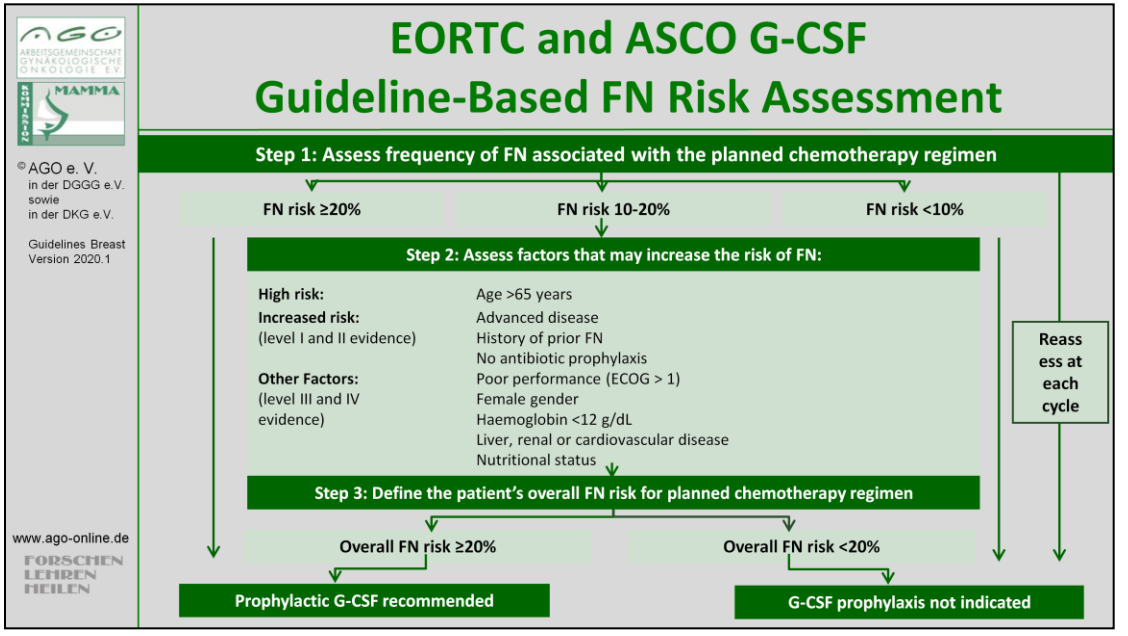

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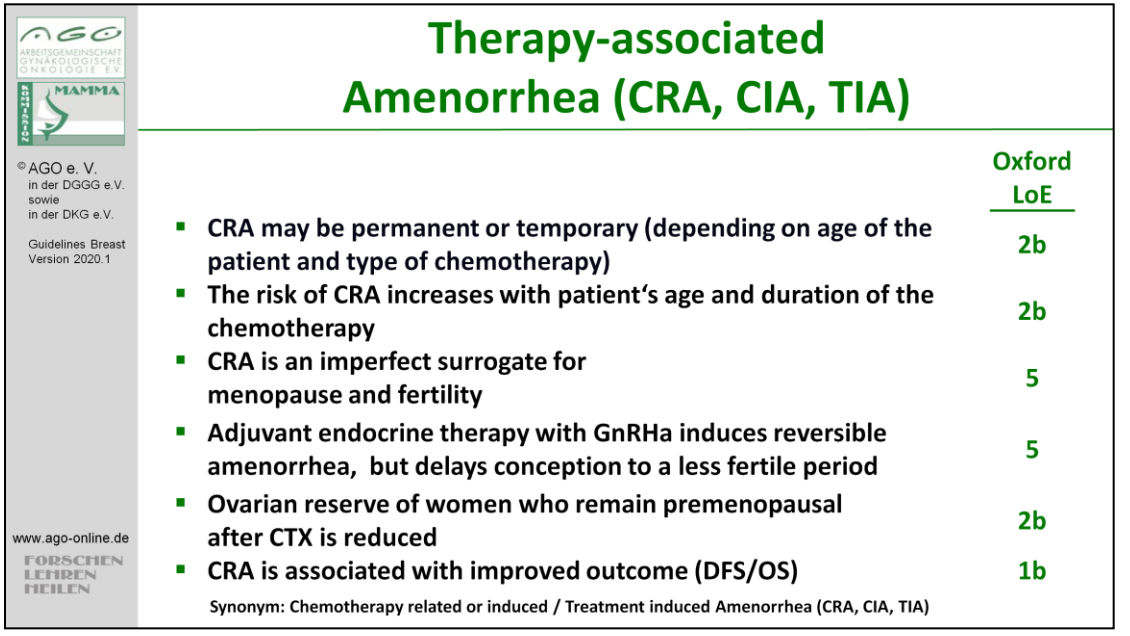
4. Endocrine disorders



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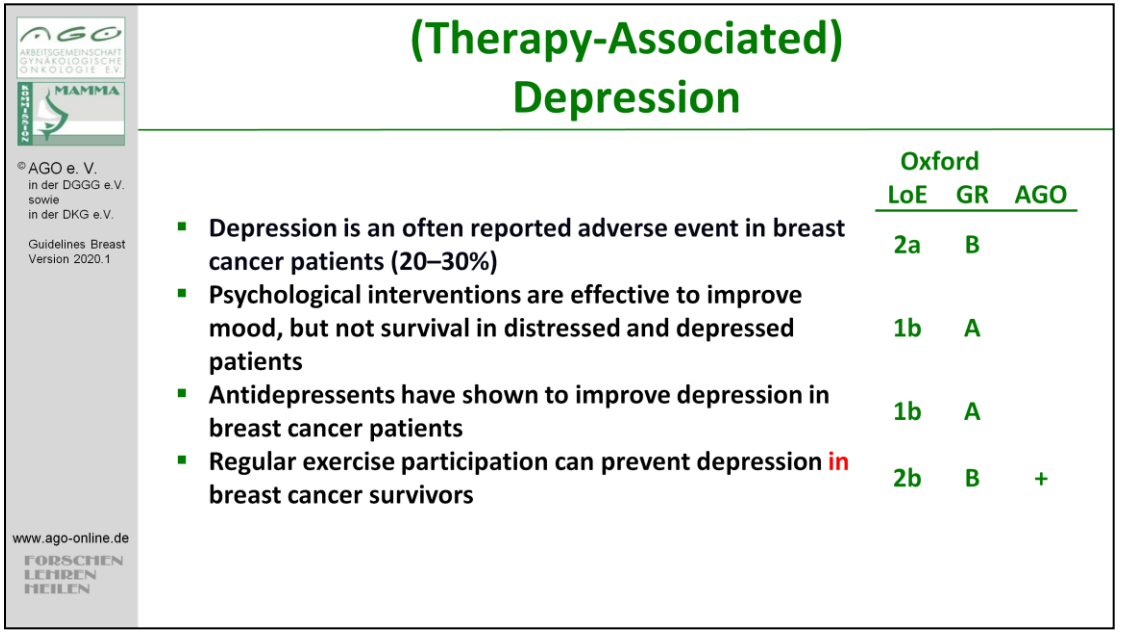
5. Psychiatric Disorders

- Depression
- Fatigue
- Cognitive impairment
- Sleep disturbances



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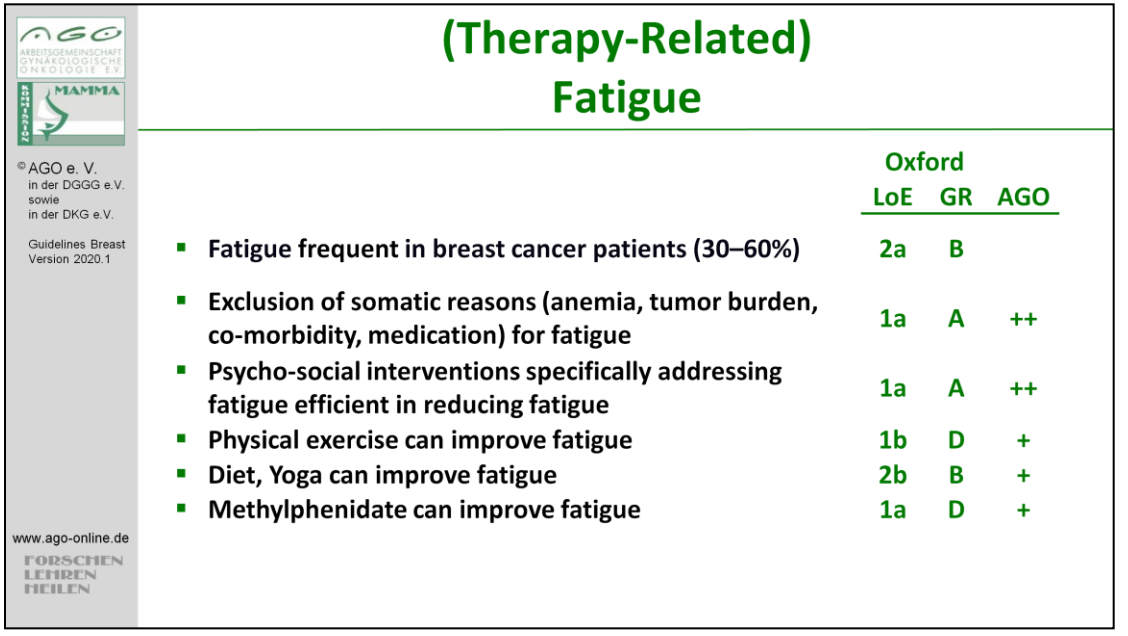

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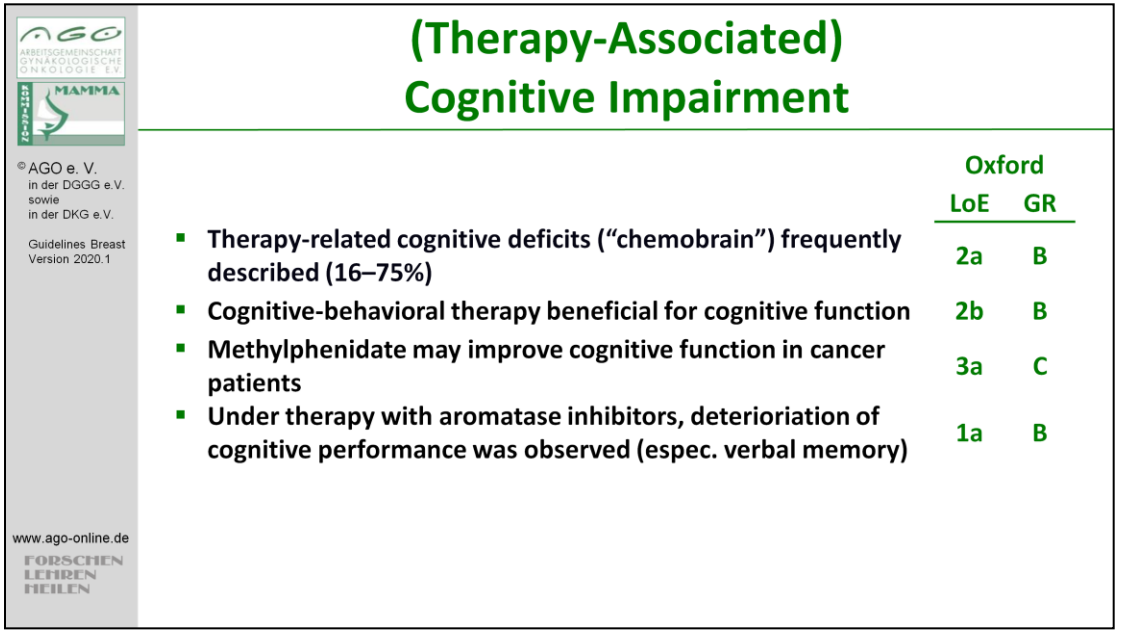

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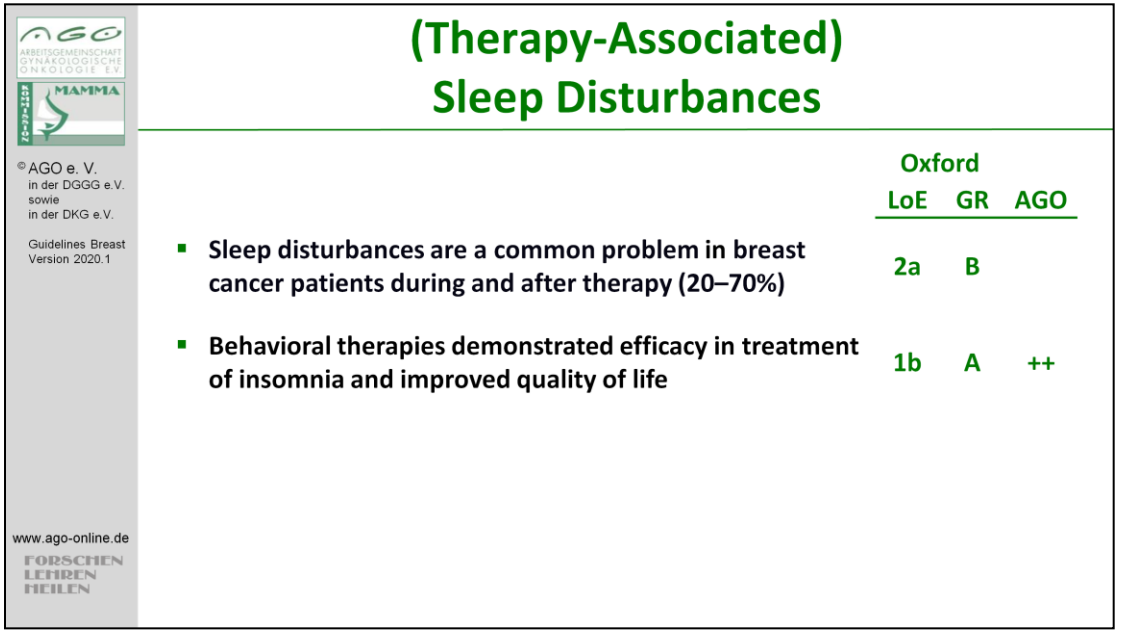

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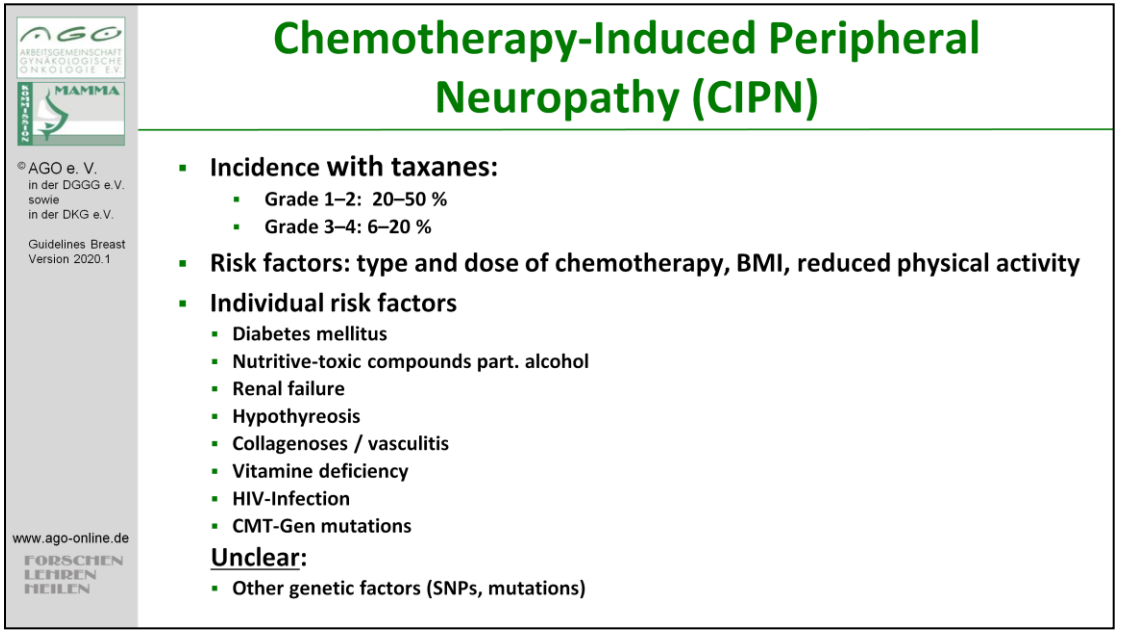
Side Effects According Organ Systems
Incidence, Prevention, Therapy

Guidelines Breast
Version 2020.1

6. Nervous system disorders

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



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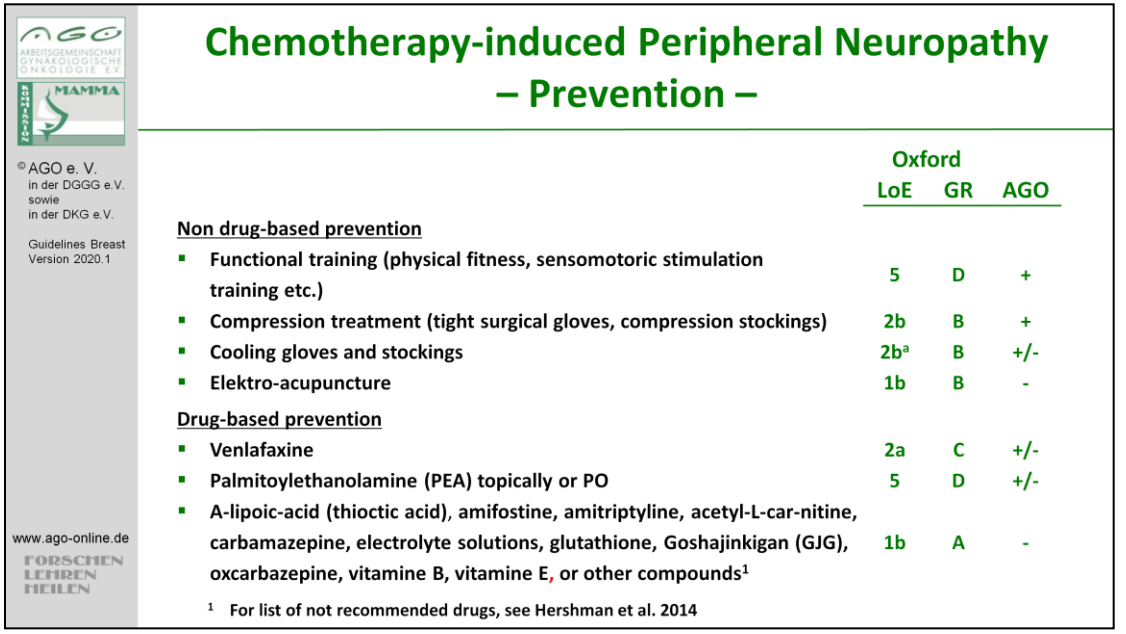

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Nicht-medikamentöse Prävention

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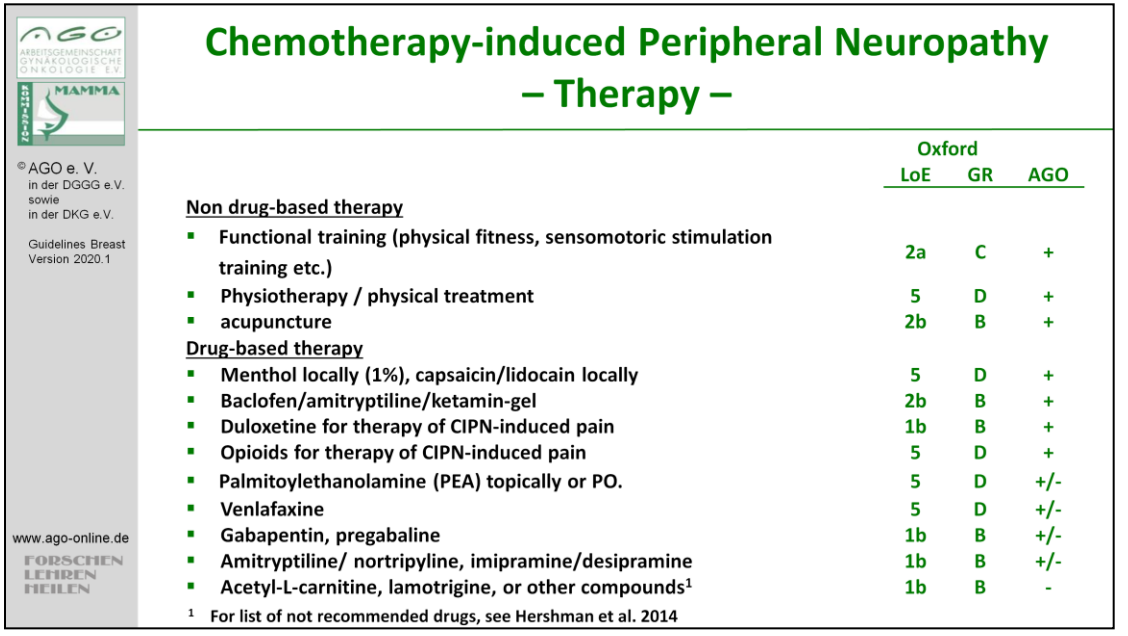

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Akupunktur:

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Guidelines Breast
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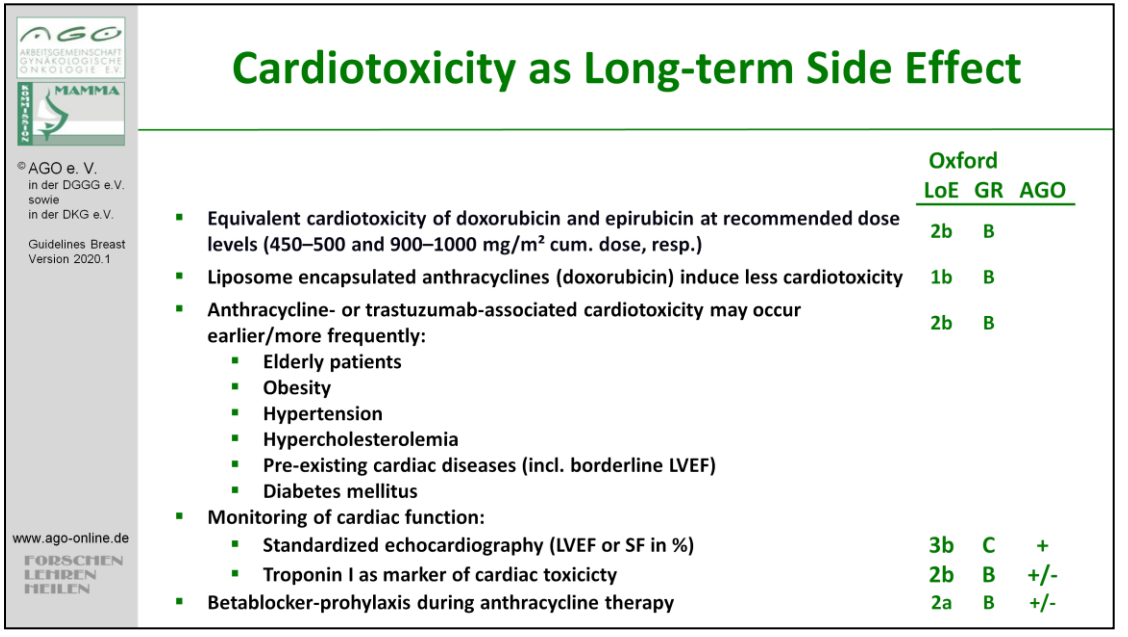
Side Effects According Organ Systems
Incidence, Prevention, Therapy

7. Cardiac Disorders



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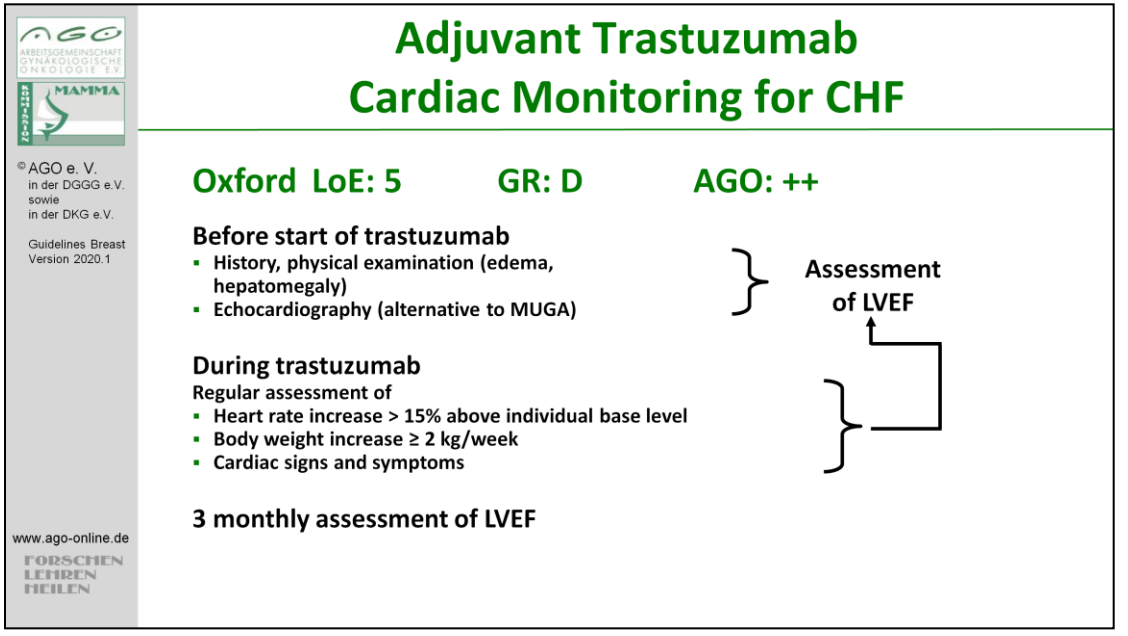

Statement: Cardiac Monitoring (5 D ++)
Vote result of the AGO recommendation: 100%

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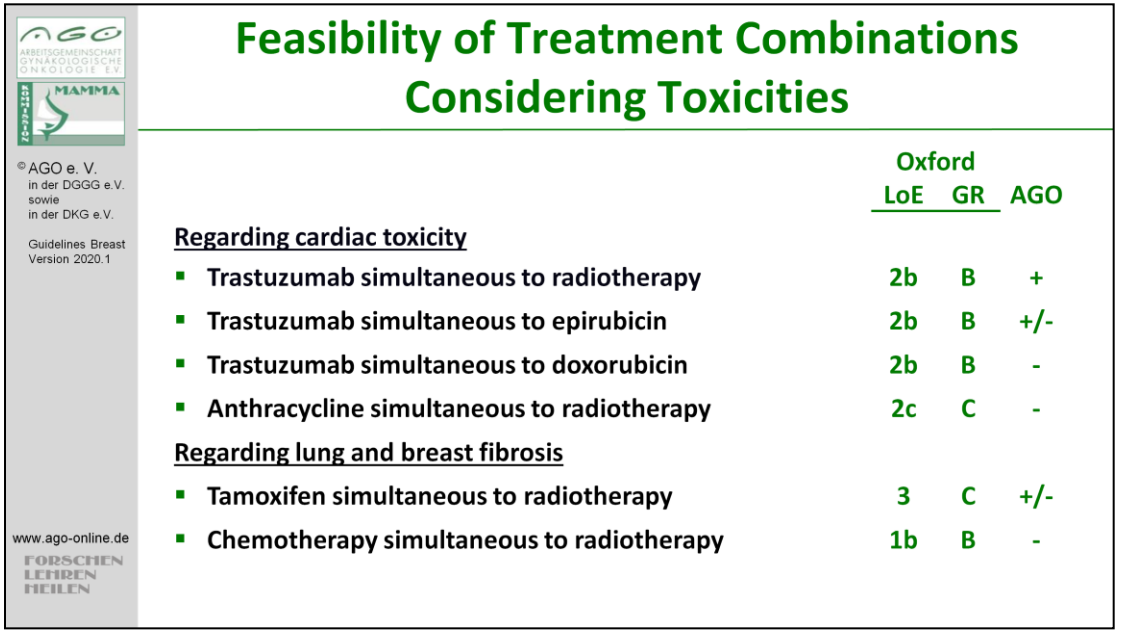

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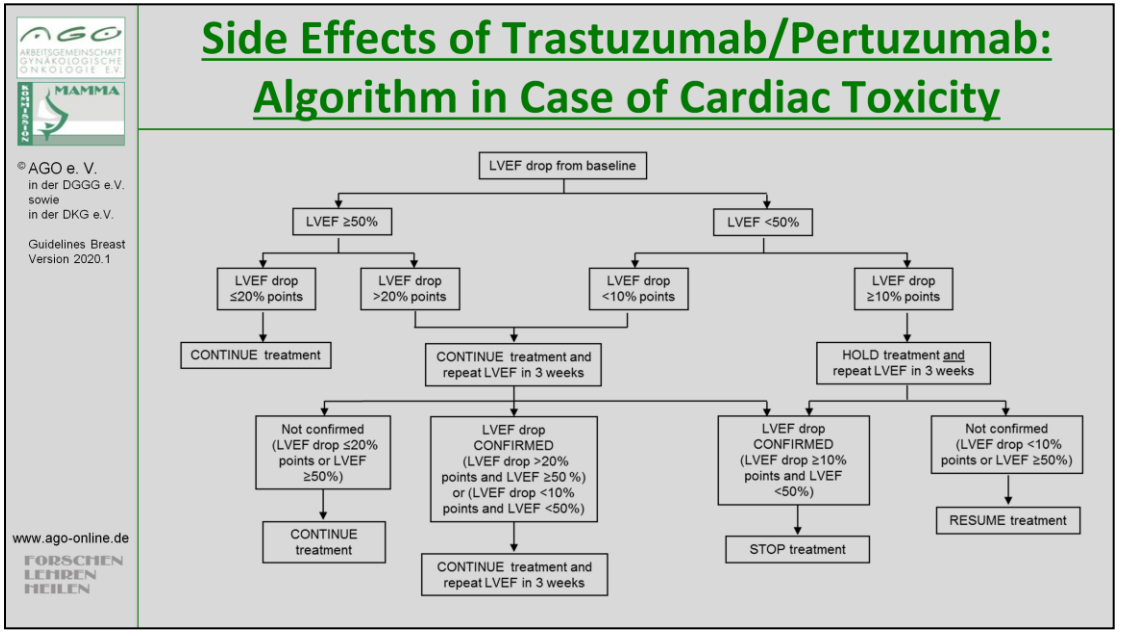

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Side Effects According Organ Systems
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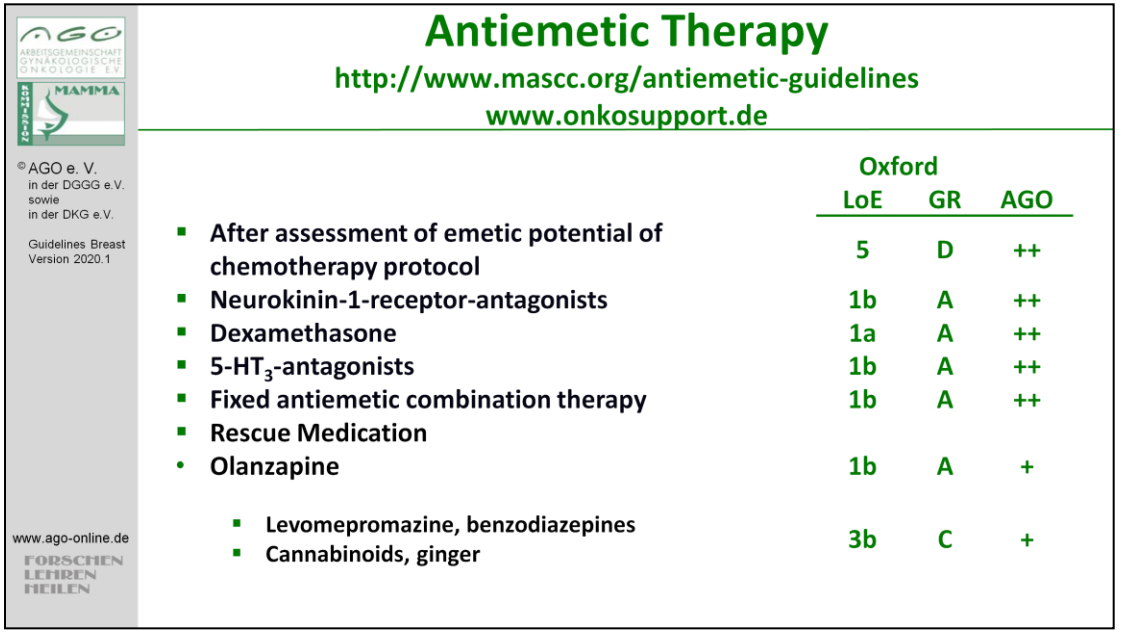
8. Gastrointestinal Disorders

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



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Olanzepine:

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Antiemetic Therapy
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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.

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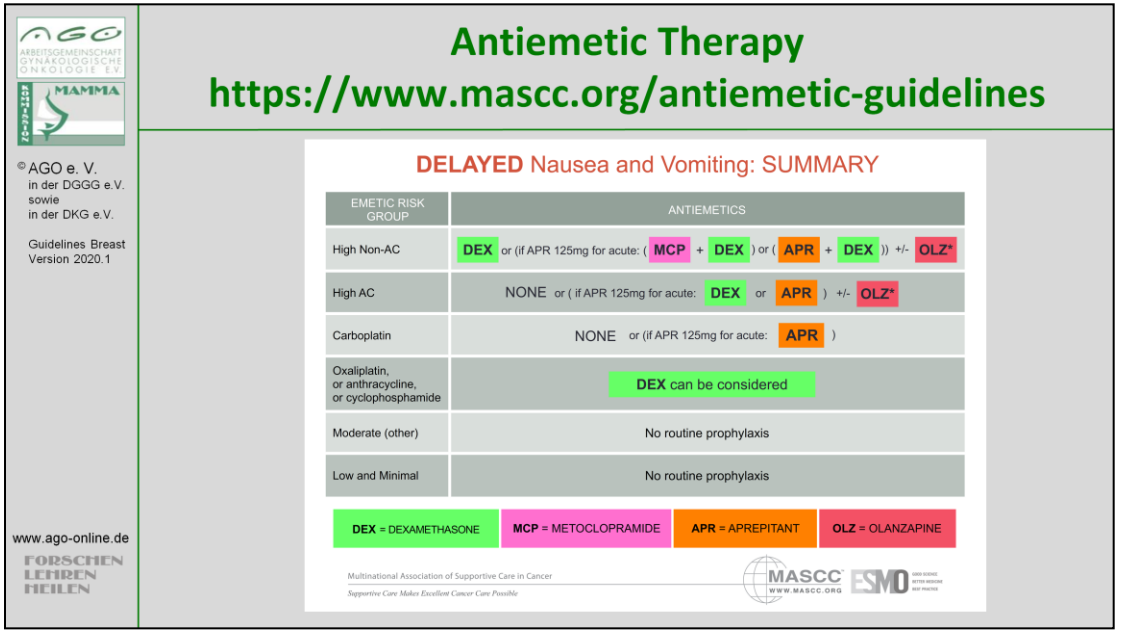
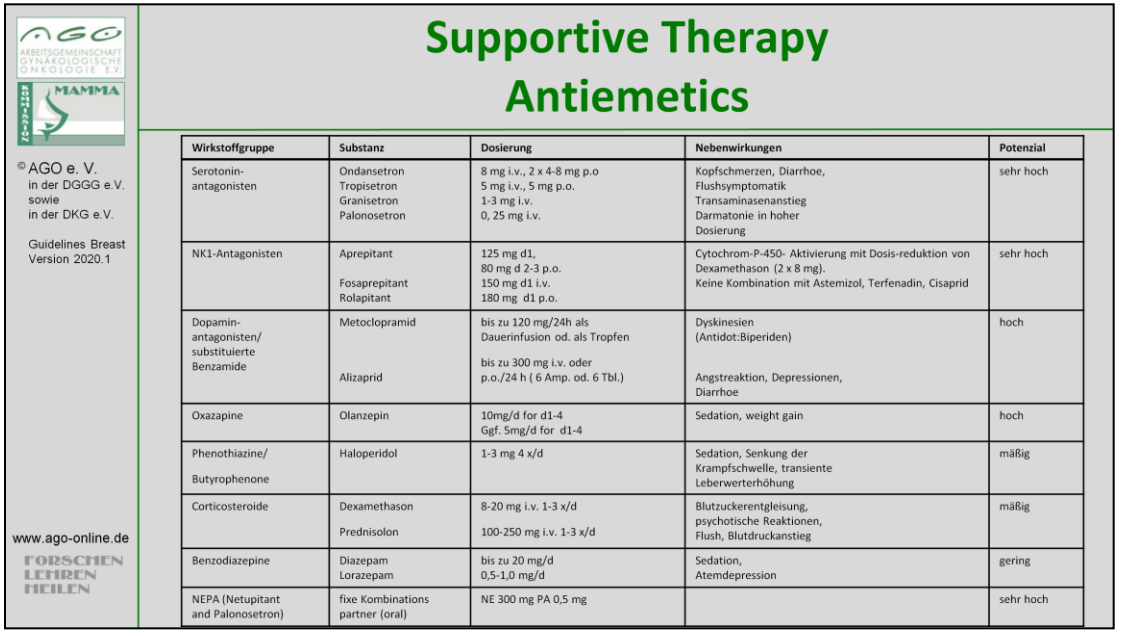
https://www.mascc.org/antiemetic-guidelines

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



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



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, Diarrhoe	hoch
Oxazapine	Olanzepin	10mg/d for d1-4 Ggf. 5mg/d for d1-4	Sedation, weight gain	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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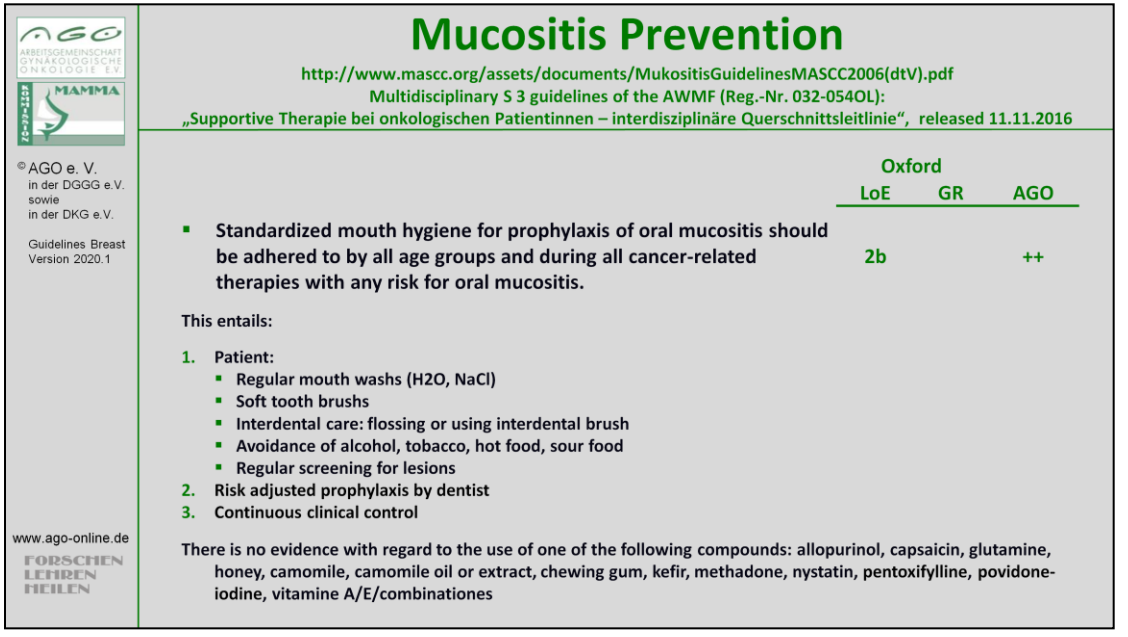
3. Hashimoto H, Abe M, Tokuyama O, et al: Olanzapine 5 mg plus standard antiemetic therapy for the prevention of chemotherapy-induced nausea and vomiting (j-force): A multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 2019.



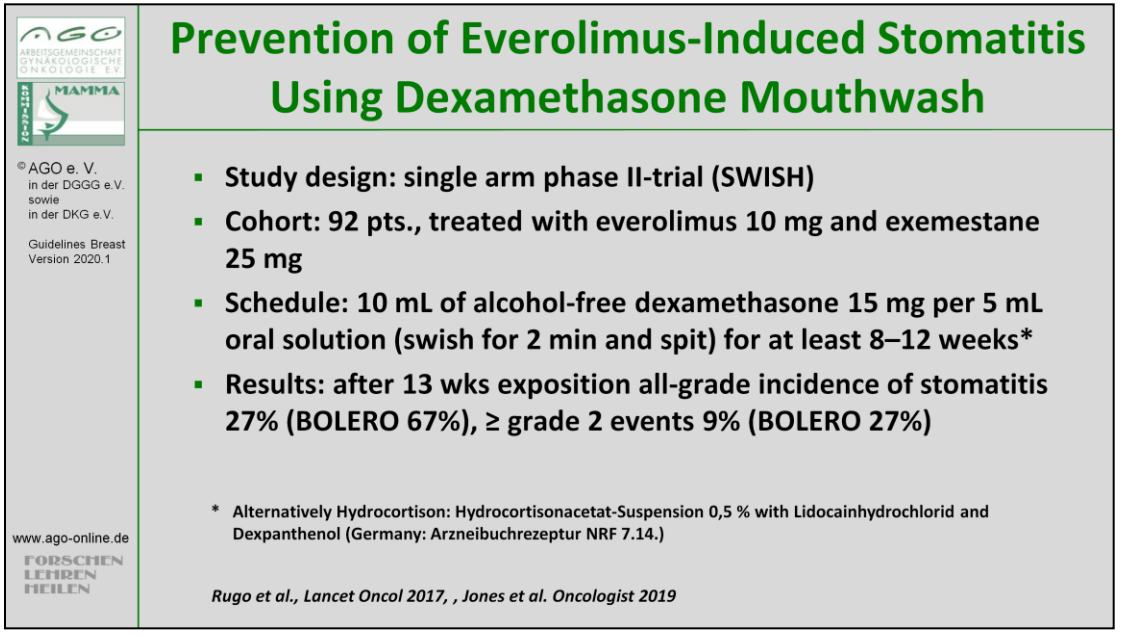
Relevant practice guideline

Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.2, 2019,

AWMF Registernummer: 032/054OL, http://leitlinienprogramm- onkologie.de/Supportive-Therapie.95.0.html (Zugriff am 08.01.2020)

1. RV Lalla, J Bowen, RV Lalla, et al.: MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. Cancer 2014; 120:1453-61
2. McGuire DB, Fulton JS, Park J, et al.: Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO). Systematic review of basic oral care for the management of oral mucositis in cancer patients. Support Care Cancer 2013 Nov;21(11):3165-77.
3. Jensen, S. B., V. Jarvis, Y. Zadik, et al.: "Systematic review of miscellaneous agents for the management of oral mucositis in cancer patients."
4. Support Care Cancer 2013;21(11): 3223-3232.
5. Leenstra, J. L., R. C. Miller, R. Qin et al.:"Doxepin rinse versus placebo in the treatment of acute oral mucositis pain in patients receiving head and neck radiotherapy with or without chemotherapy: a phase III, randomized, double-blind trial (NCCTG-N09C6

[Alliance]). J Clin Oncol 2014;32(15): 1571-1577.
6. Nicolatou-Galitis, O., T. Sarri, J. Bowen, et al.: Systematic review of amifostine for the management of oral mucositis in cancer patients. Support Care Cancer 2013; 21(1): 357-364.
7. Peterson, D. E., K. Ohrn, J. Bowen, et al.: Systematic review of oral cryotherapy for management of oral mucositis caused by cancer therapy. Support Care Cancer 2013; 21(1): 327-332.
8. Saunders, D. P., J. B. Epstein, S. Elad, J, et al.: Systematic review of antimicrobials, mucosal coating agents, anesthetics, and analgesics for the management of oral mucositis in cancer patients. Support Care Cancer 2013; 21(11): 3191-3207.
9. Yarom, N., A. Ariyawardana, A. Hovan, et al.: Systematic review of natural agents for the management of oral mucositis in cancer patients. Support Care Cancer 2013;21(11):3209-21.



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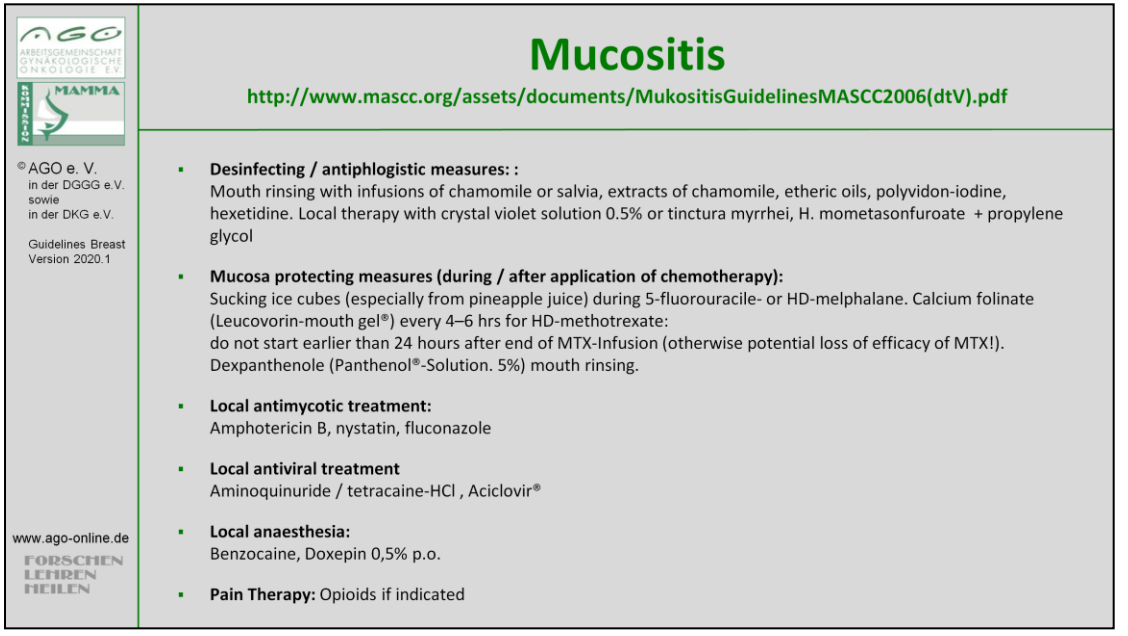

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3. McGuire DB, Fulton JS, Park J, et al; Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO). Systematic review of basic oral care for the management of oral mucositis in cancer patients. Support Care Cancer 2013 Nov;21(11):3165-77.
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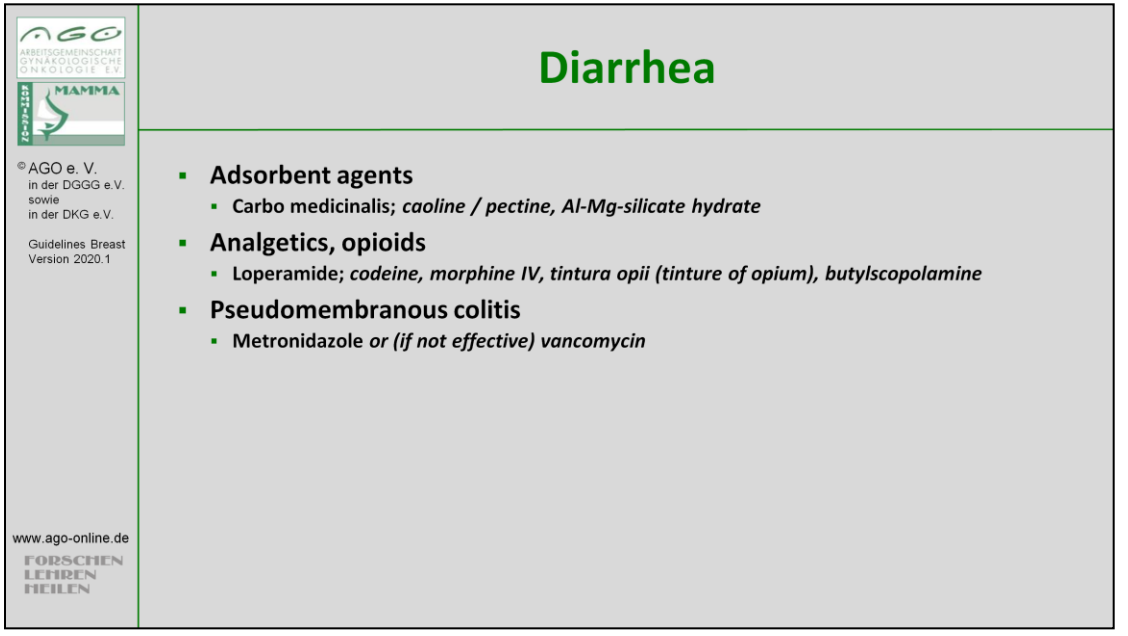

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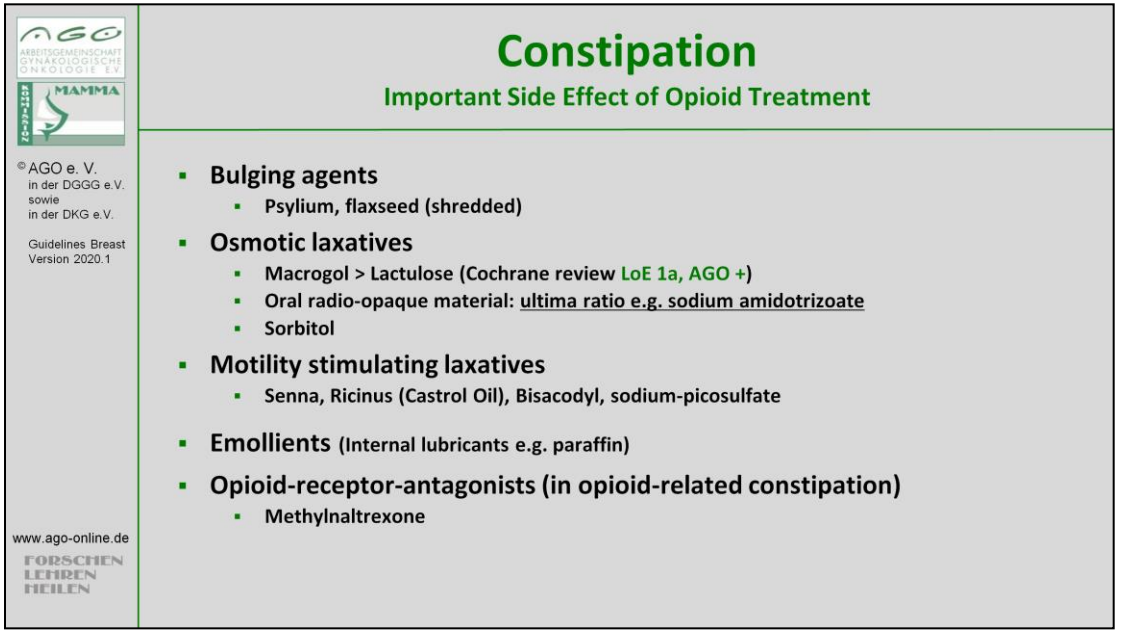

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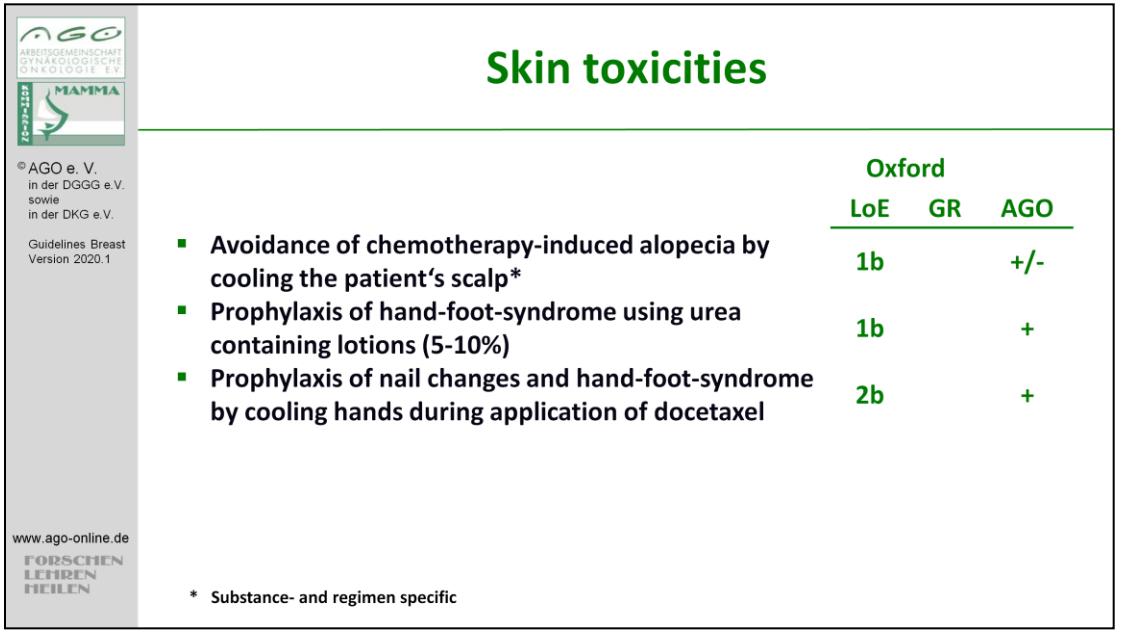
Guidelines Breast
Version 2020.1

9. Skin & Subcutaneous Tissue Disorders (Alopecia)



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Scalp Cooling:

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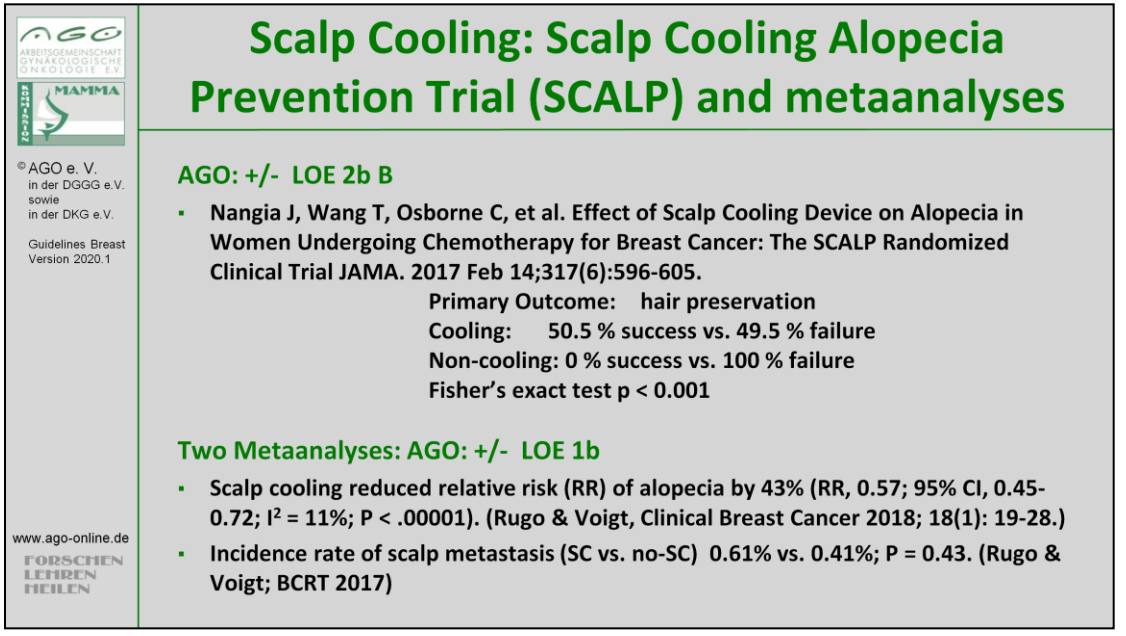

1. Nangia J, Wang T, Osborne C, et al. Effect of Scalp Cooling Device on Alopecia in Women Undergoing Chemotherapy for Breast Cancer: The SCALP Randomized Clinical Trial JAMA. 2017 Feb 14;317(6):596-605.
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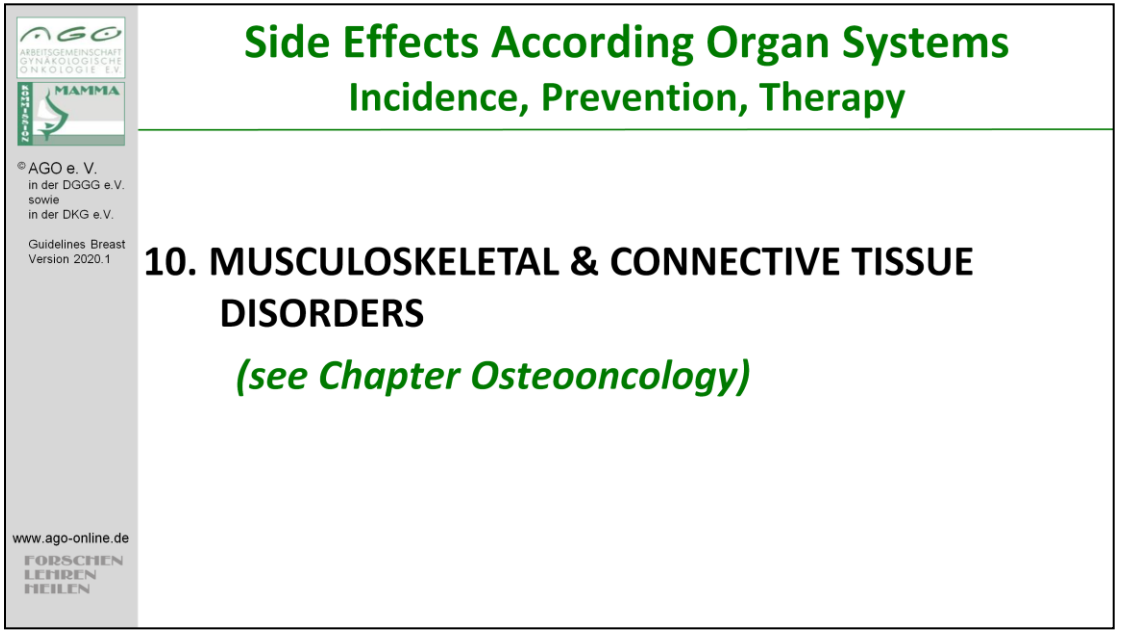

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Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.2, 2019,

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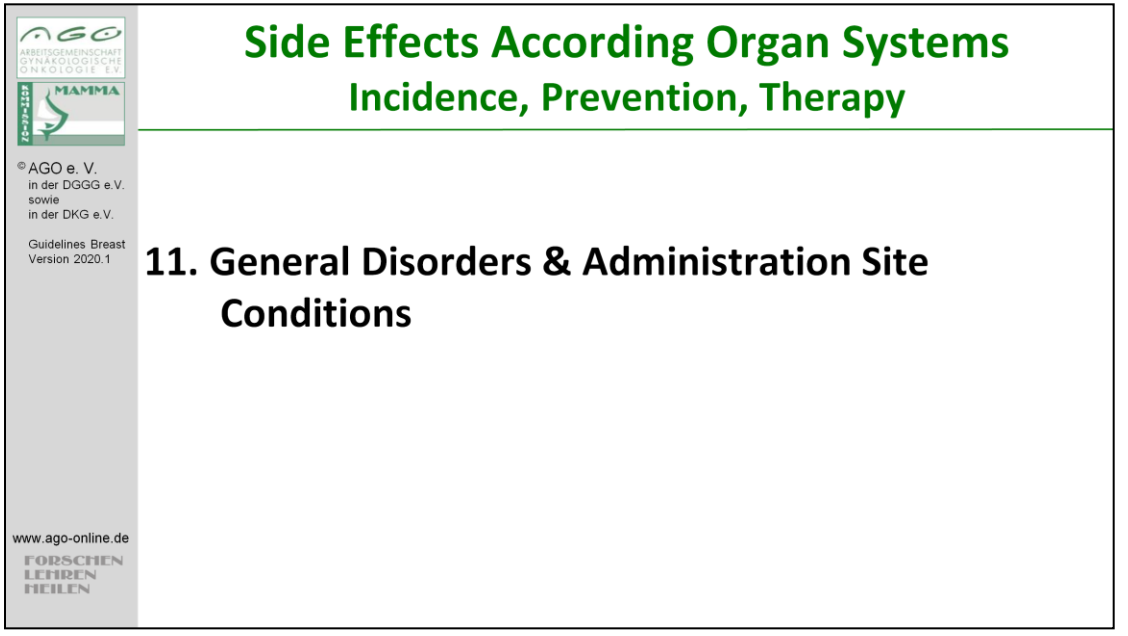

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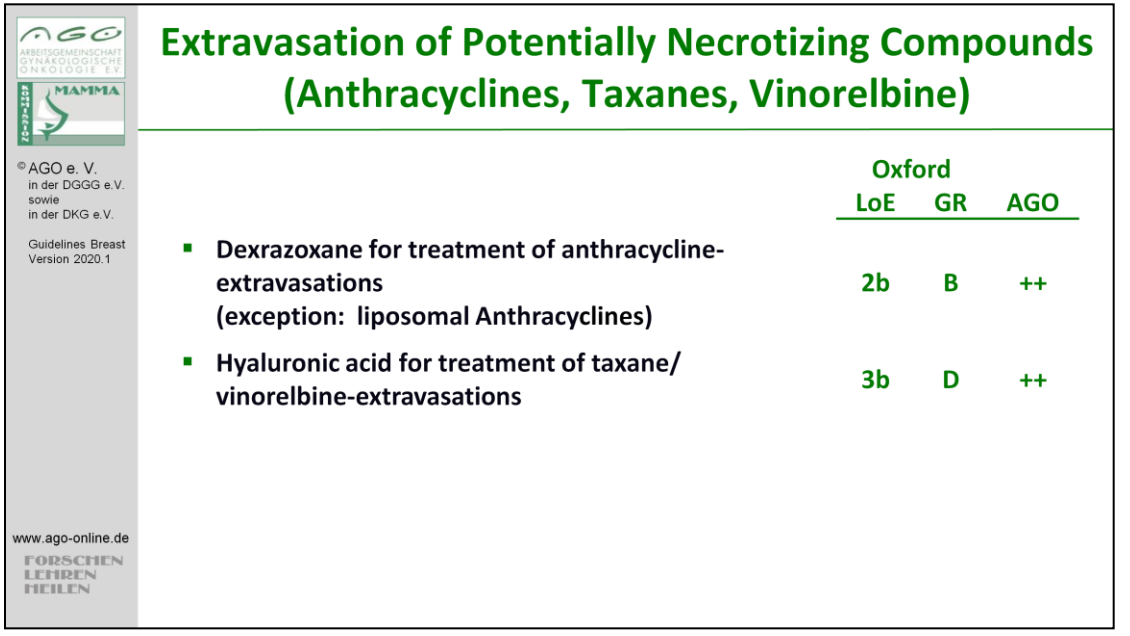

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Dexrazoxane

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Hyaluronsäure

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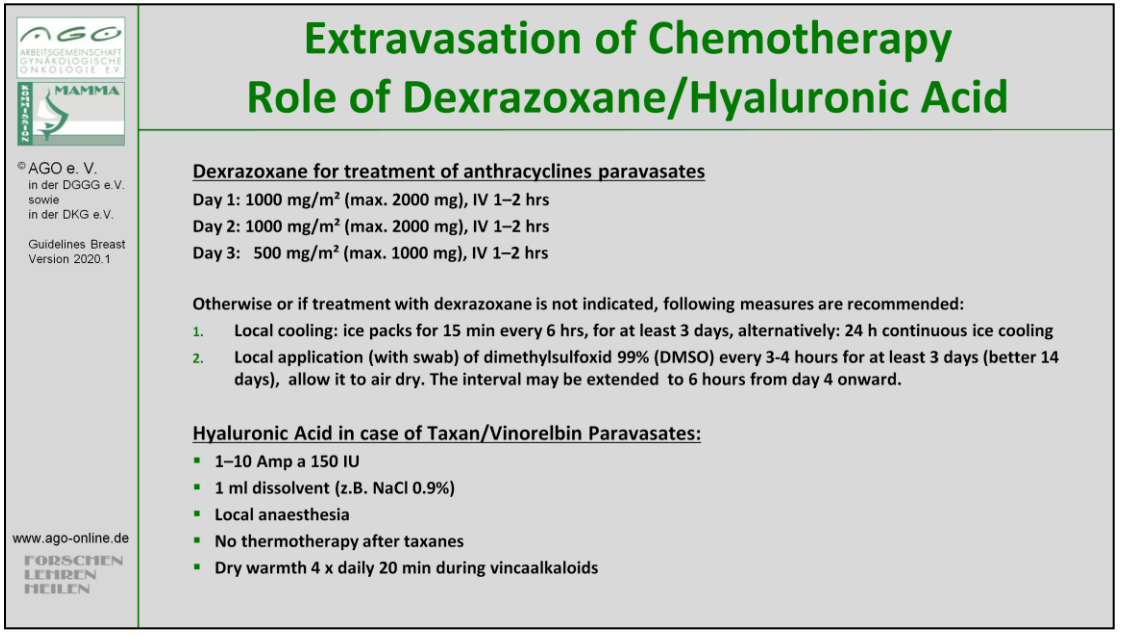

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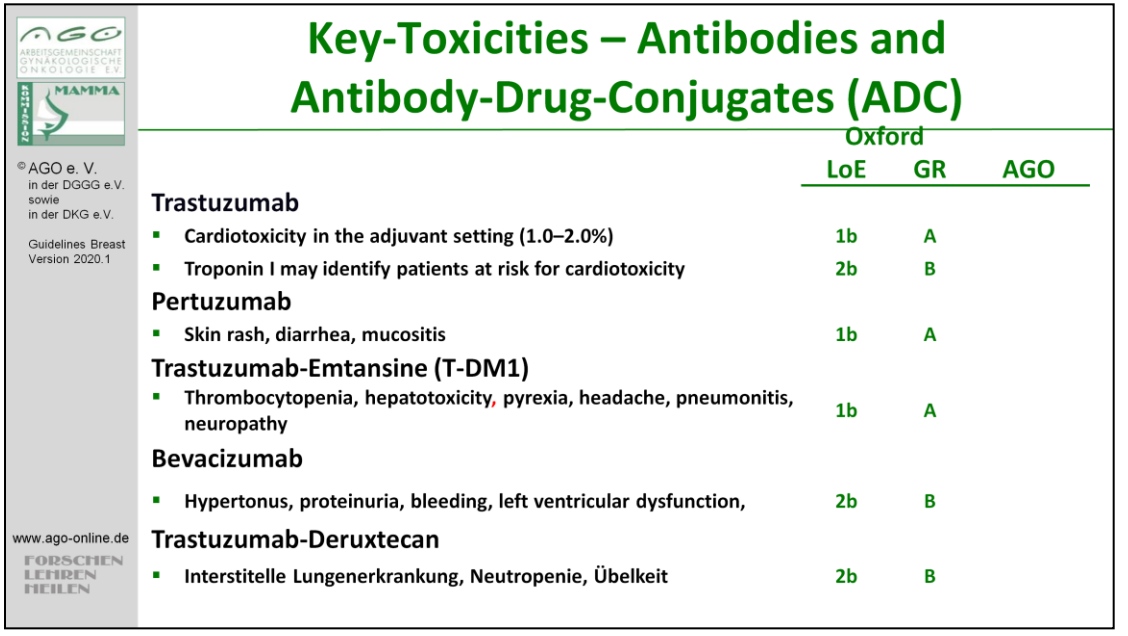
Substance-Specific Side Effects

- Antibodies and Antibody-Drug-Conjugates (ADC)
- CDK 4/6-Inhibitors
- PARP-Inhibitors
- Small molecules (TKI, mTOR.Inihibitor)
- Immun-Checkpoint-Antibodies
- PI3-Kinase-Inhibitoren (Alpelisib)



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T-DM1

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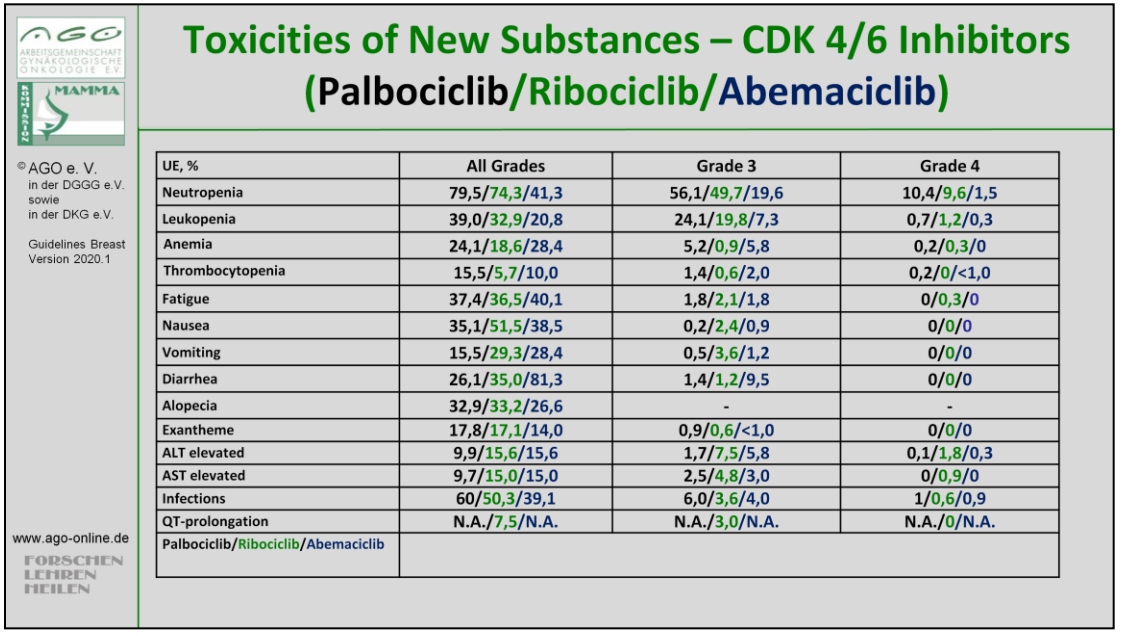

UE, %	All Grades	Grade 3	Grade 4
Neutropenia	79,5/74,3/41,3	56,1/49,7/19,6	10,4/9,6/1,5
Leukopenia	39,0/32,9/20,8	24,1/19,8/7,3	0,7/1,2/0,3
Anemia	24,1/18,6/28,4	5,2/0,9/5,8	0,2/0,3/0
Thrombocytopenia	15,5/5,7/10,0	1,4/0,6/2,0	0,2/0/<1,0
Fatigue	37,4/36,5/40,1	1,8/2,1/1,8	0/0,3/0
Nausea	35,1/51,5/38,5	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

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.
2. N.Harbeck, J. Ettl, Palbociclib, CDK 4/ 6 Inhibition als neue Therapieoption bei Patientinnen mit fortgeschrittenem HR+/ Her – Mammakarzinom. Drug Report, 2017

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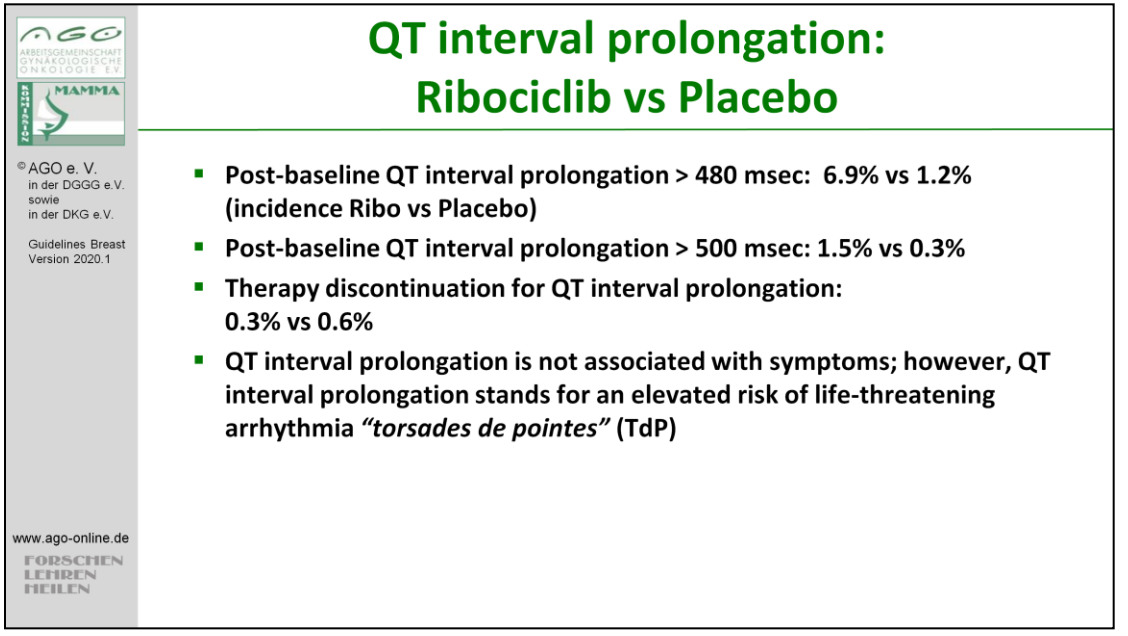
1. Hortobagyi GN, Stemmer SM, Burris HA, et al. Ribociclib as First-Line Therapy for HR-Positive, Advanced Breast Cancer. N Engl J Med. 2016 Nov 3;375(18):1738-1748. Epub 2016 Oct 7.

Abemaciclib

1. Sledge GW, Jr., Toi M, Neven P, et al: Monarch 2: Abemaciclib in combination with fulvestrant in women with hr+/her2- advanced breast cancer who had progressed while receiving endocrine therapy. J Clin Oncol 2017;35:2875-2884.
2. Goetz MP, Toi M, Campone M, et al: Monarch 3: Abemaciclib as initial therapy for advanced breast cancer. J Clin Oncol 2017;35:3638-3646.



1. Tripathy D, Im SA, Colleoni M, et al. Ribociclib plus endocrine therapy for premenopausal women with hormone-receptor-positive, advanced breast cancer (MONALEESA-7): a randomized phase 3 trial. Lancet Oncol. 2018 Jul;19(7):904-915.
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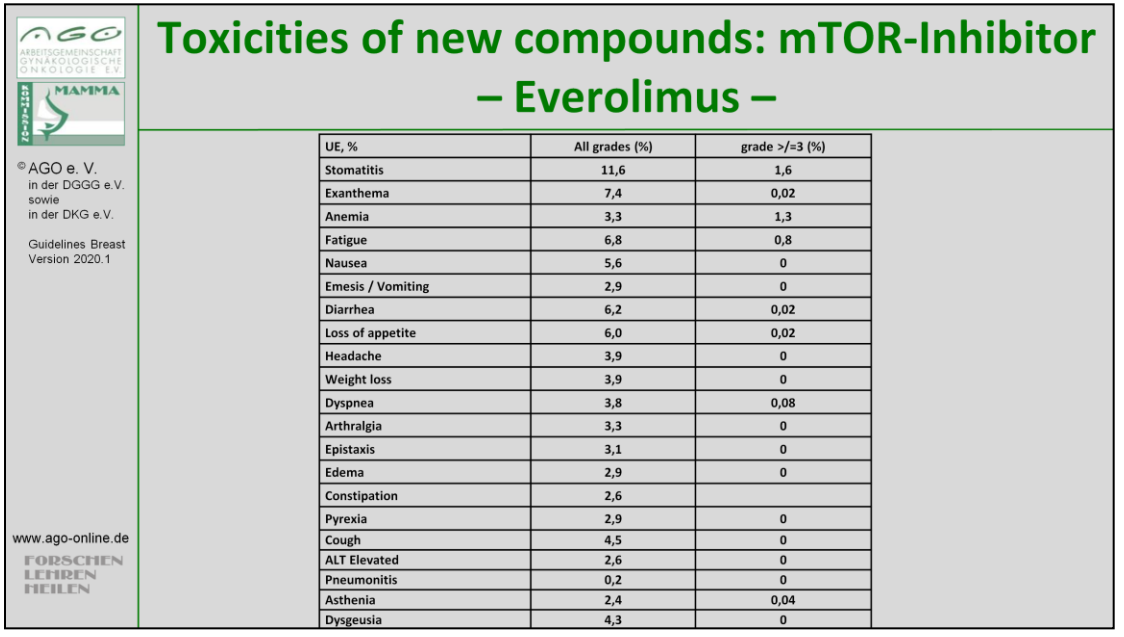
3. Durairaj C, Ruiz-Garcia A, Gauthier ER, et al. Palbociclib has no clinically relevant effect on the QTc interval in patients with advanced breast cancer. Anticancer Drugs. 2018 Mar;29(3):271-280.
4. Trinkley KE, Page RL 2nd, Lien H, et al. QT interval prolongation and the risk of torsades de pointes: essentials for clinicians. Curr Med Res Opin. 2013 Dec;29(12):1719-26.



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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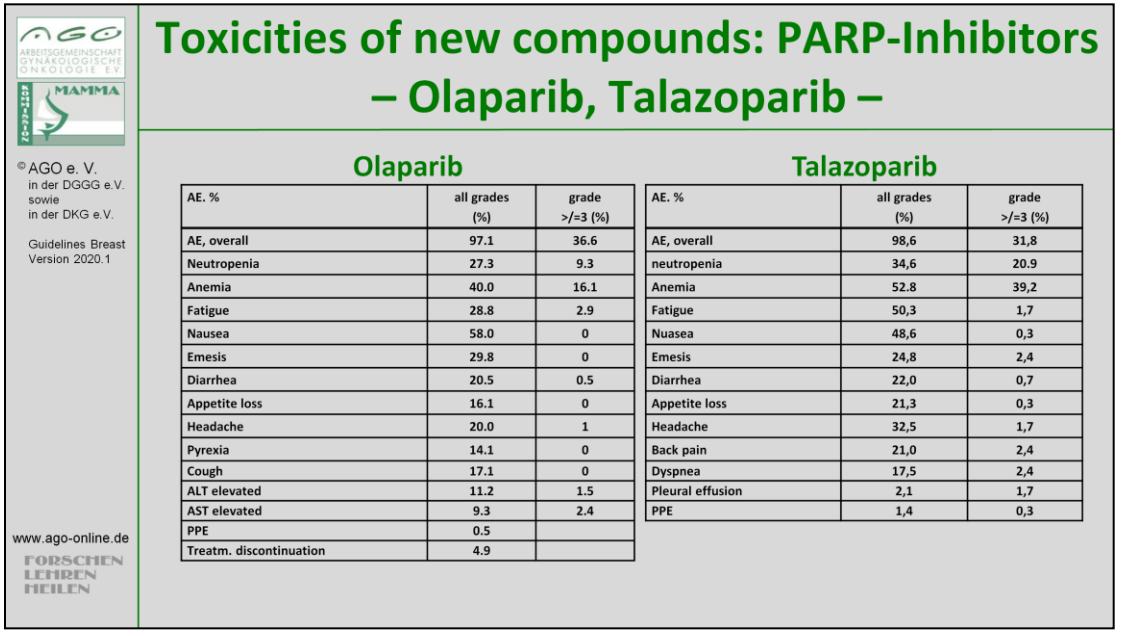

Olaparib

AE. %	all grades (%)	grade >/=3 (%)
AE, overall	97.1	36.6
Neutropenia	27.3	9.3
Anemia	40.0	16.1
Fatigue	28.8	2.9
Nausea	58.0	0
Emesis	29.8	0
Diarrhea	20.5	0.5
Appetite loss	16.1	0
Headache	20.0	1
Pyrexia	14.1	0
Cough	17.1	0
ALT elevated	11.2	1.5
AST elevated	9.3	2.4
PPE	0.5	
Treatm. discontinuation	4.9	

Talazoparib

AE. %	all grades (%)	grade >/=3 (%)
AE, overall	98,6	31,8
neutropenia	34,6	20.9
Anemia	52.8	39,2
Fatigue	50,3	1,7
Nuasea	48,6	0,3
Emesis	24,8	2,4
Diarrhea	22,0	0,7
Appetite loss	21,3	0,3
Headache	32,5	1,7
Back pain	21,0	2,4
Dyspnea	17,5	2,4
Pleural effusion	2,1	1,7
PPE	1,4	0,3

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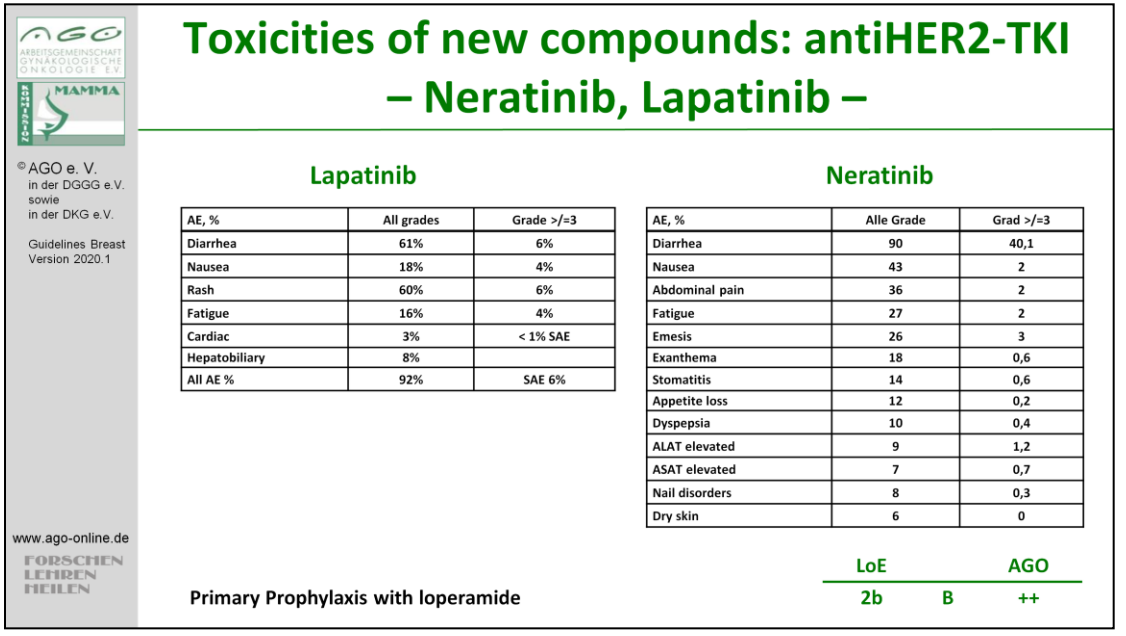

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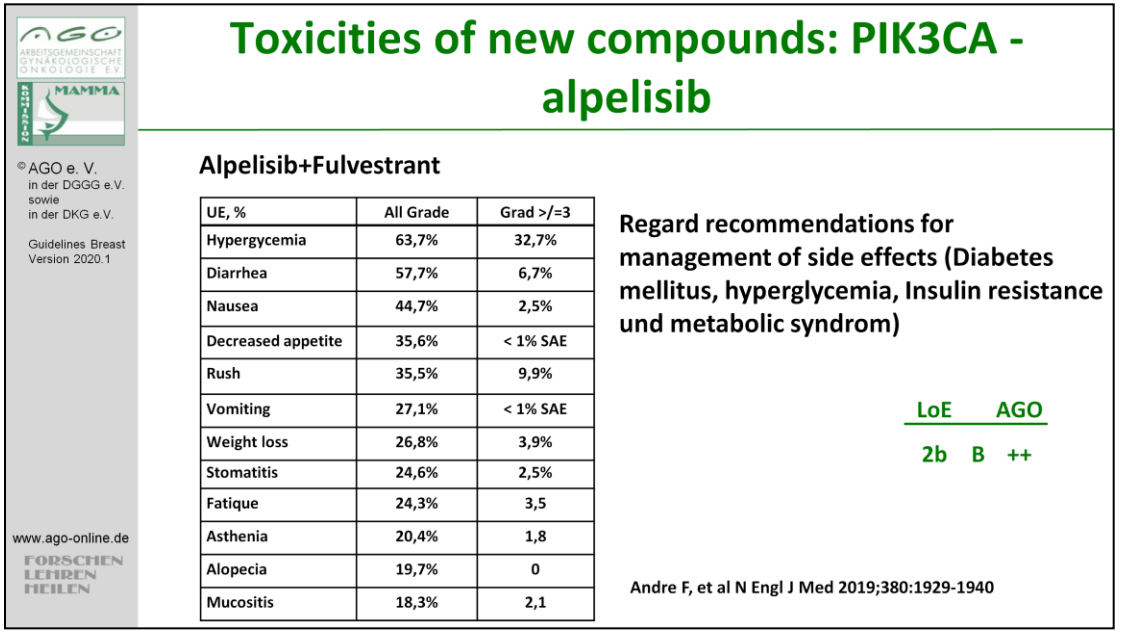

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2. Andre F, Ciruelos E, Rubovszky G et al.:Alpelisib for pik3ca-mutated, hormone receptor-positive advanced breast cancer. N Engl J Med 2019;380:1929-1940.
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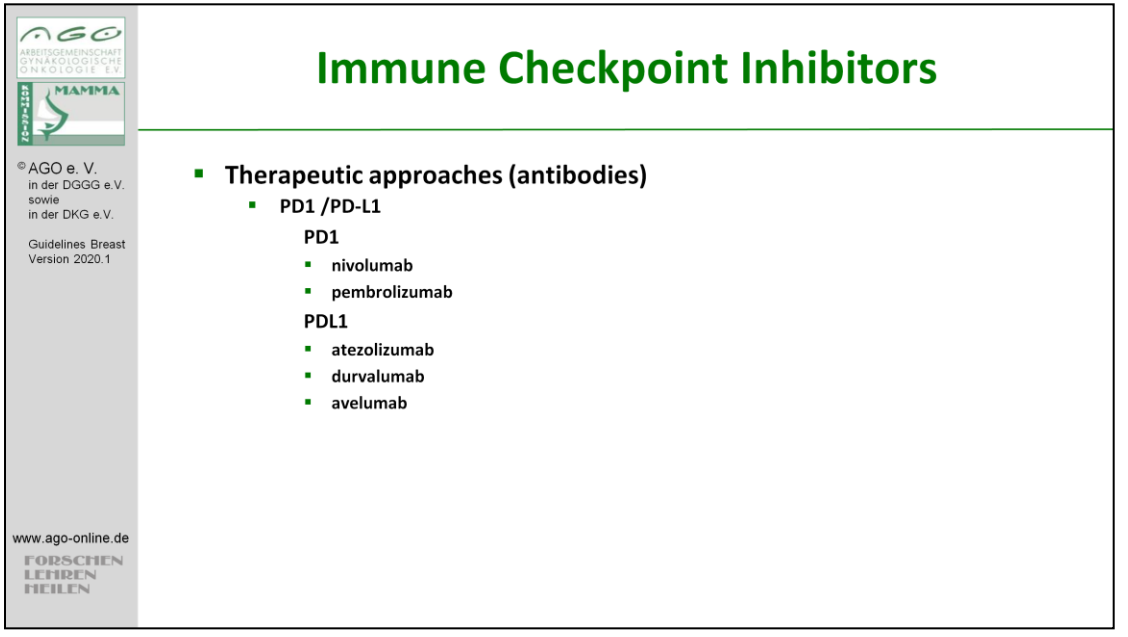

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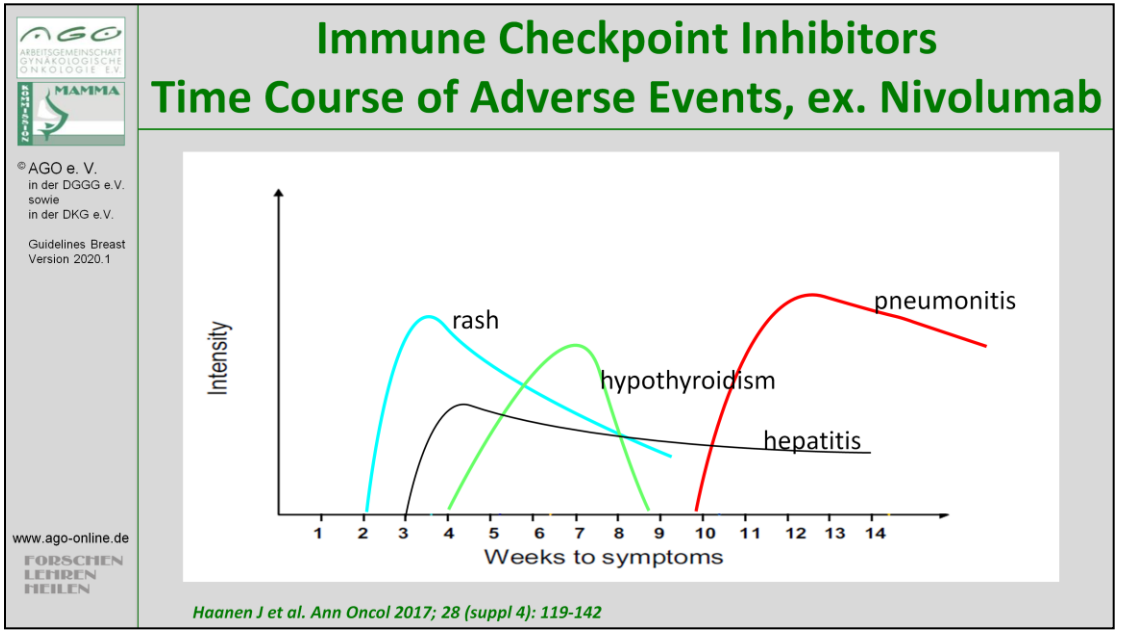

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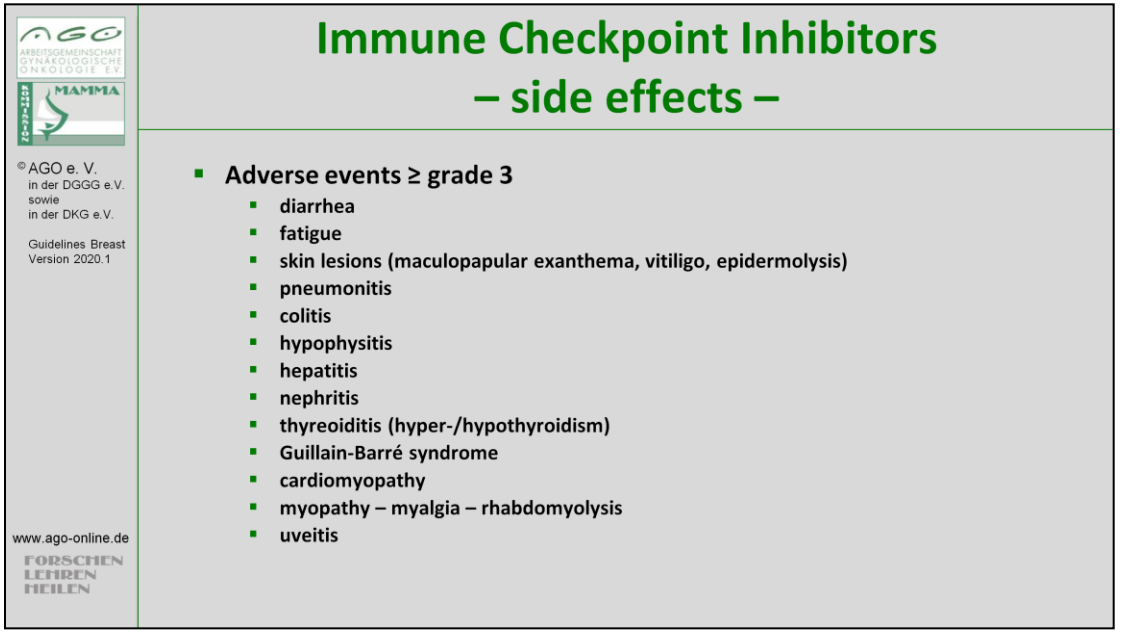

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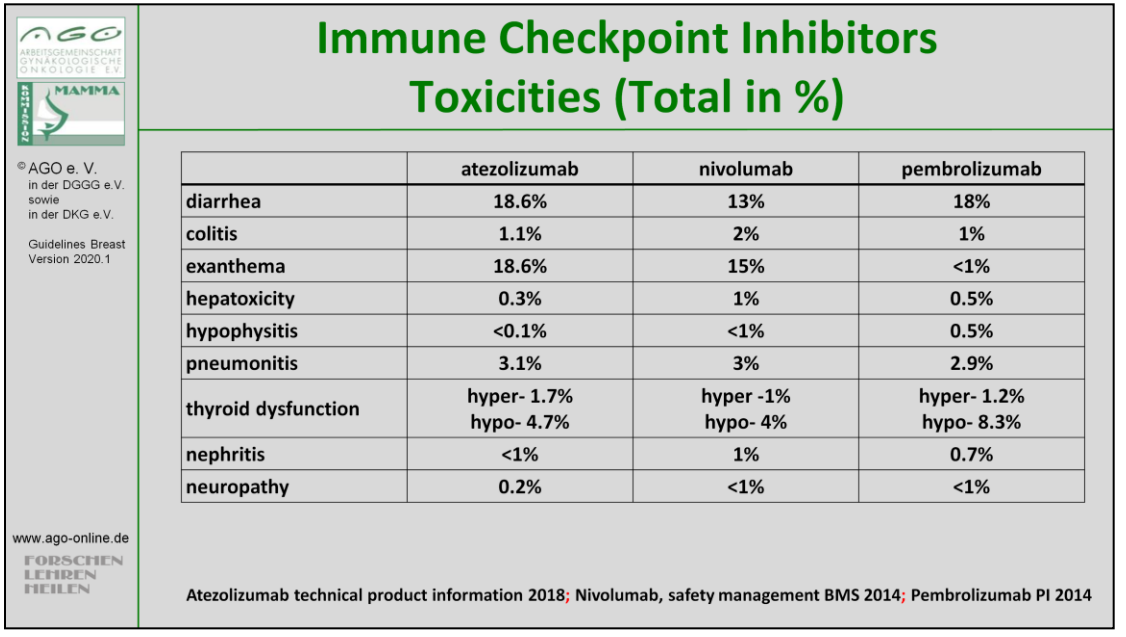


Immune Checkpoint Inhibitors Toxicities (Total in %)

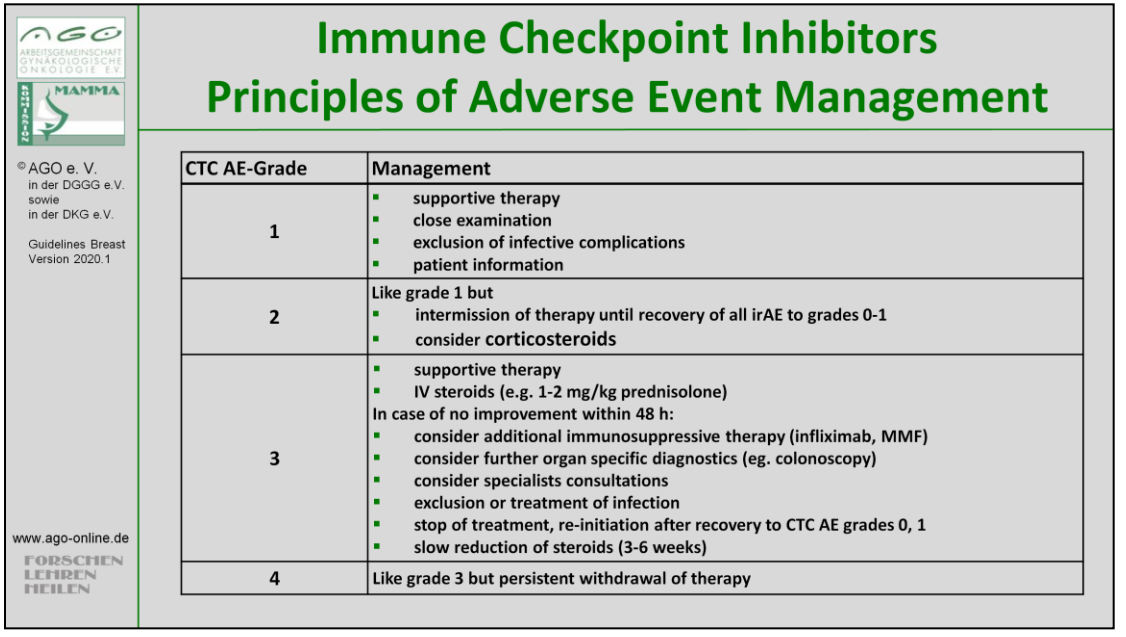
	atezolizumab	nivolumab	pembrolizumab
diarrhea	18.6%	13%	18%
colitis	1.1%	2%	1%
exanthema	18.6%	15%	<1%
hepatoxicity	0.3%	1%	0.5%
hypophysitis	<0.1%	<1%	0.5%
pneumonitis	3.1%	3%	2.9%
thyroid dysfunction	hyper- 1.7% hypo- 4.7%	hyper -1% hypo- 4%	hyper- 1.2% hypo- 8.3%
nephritis	<1%	1%	0.7%
neuropathy	0.2%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

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

Atezolizumab: https://www.fachinfo.de/suche/fi/021700

Nivolumab: https://www.fachinfo.de/suche/fi/020675

Pembrolizumab: https://www.fachinfo.de/suche/fi/020716



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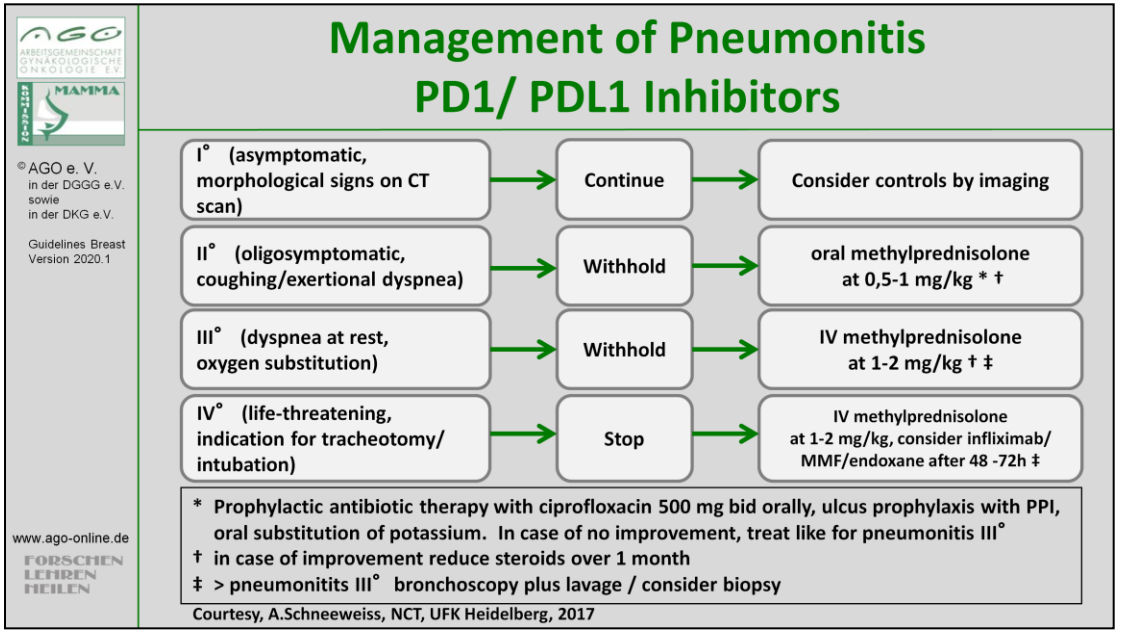

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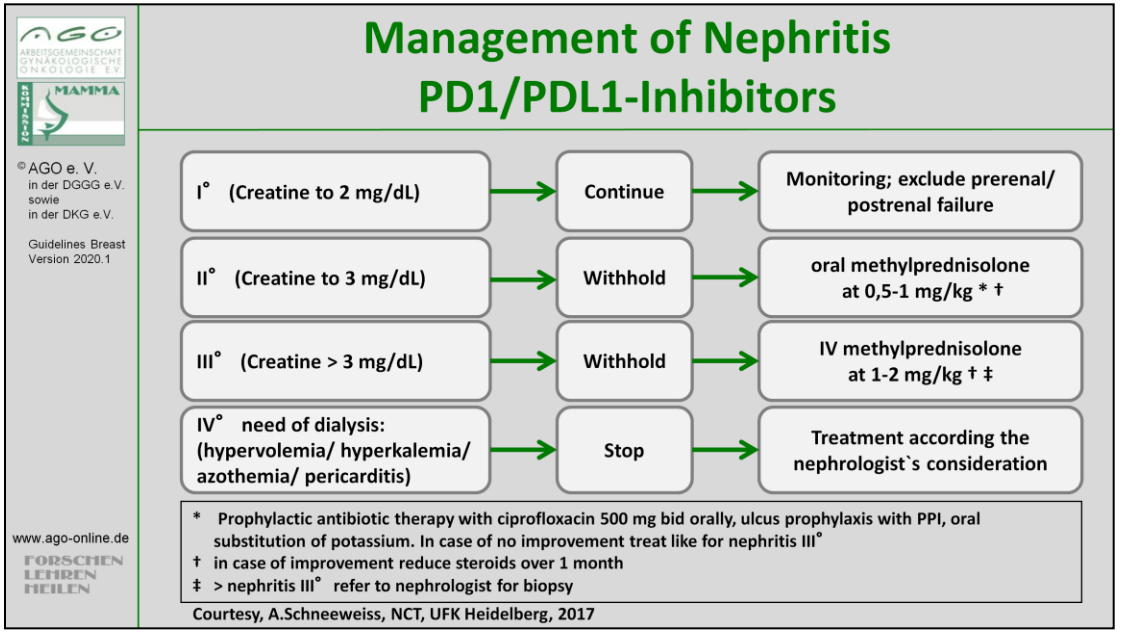

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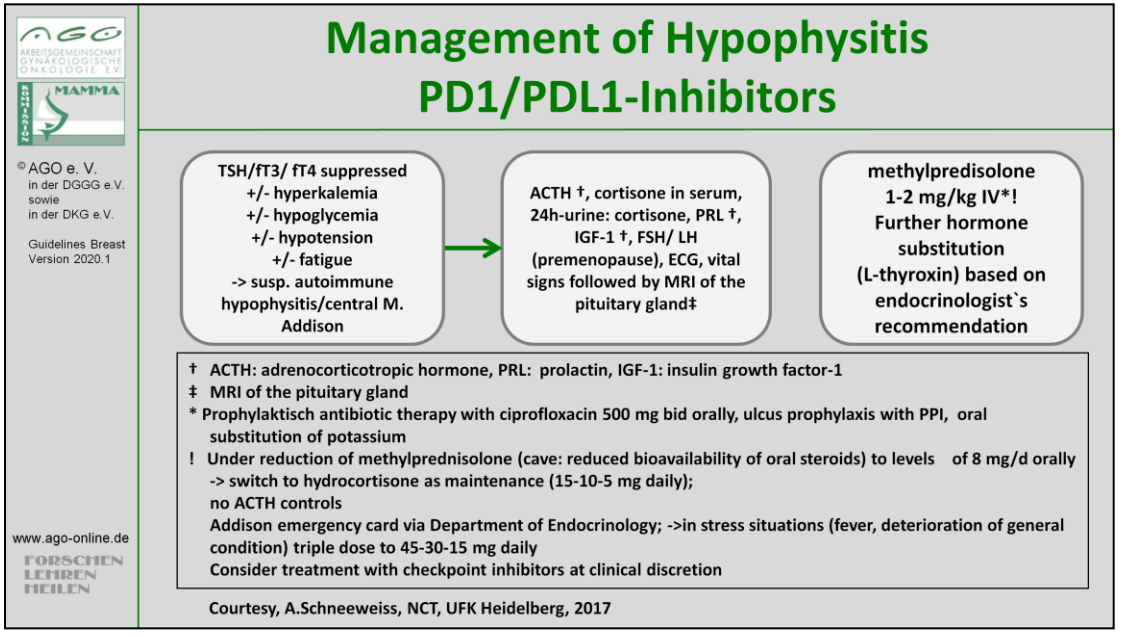

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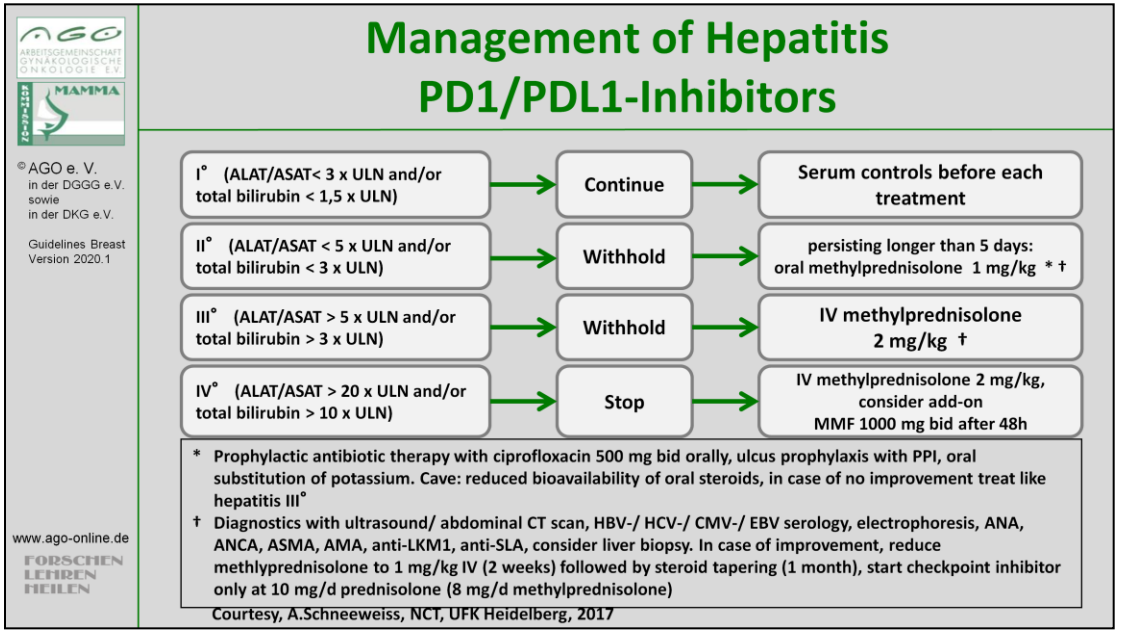

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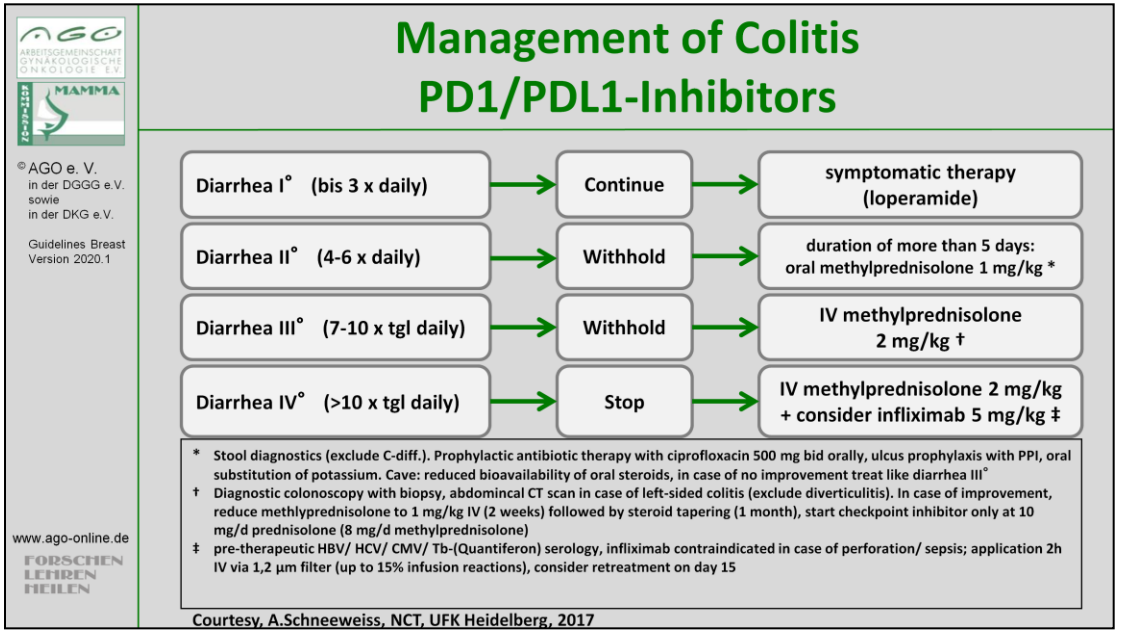

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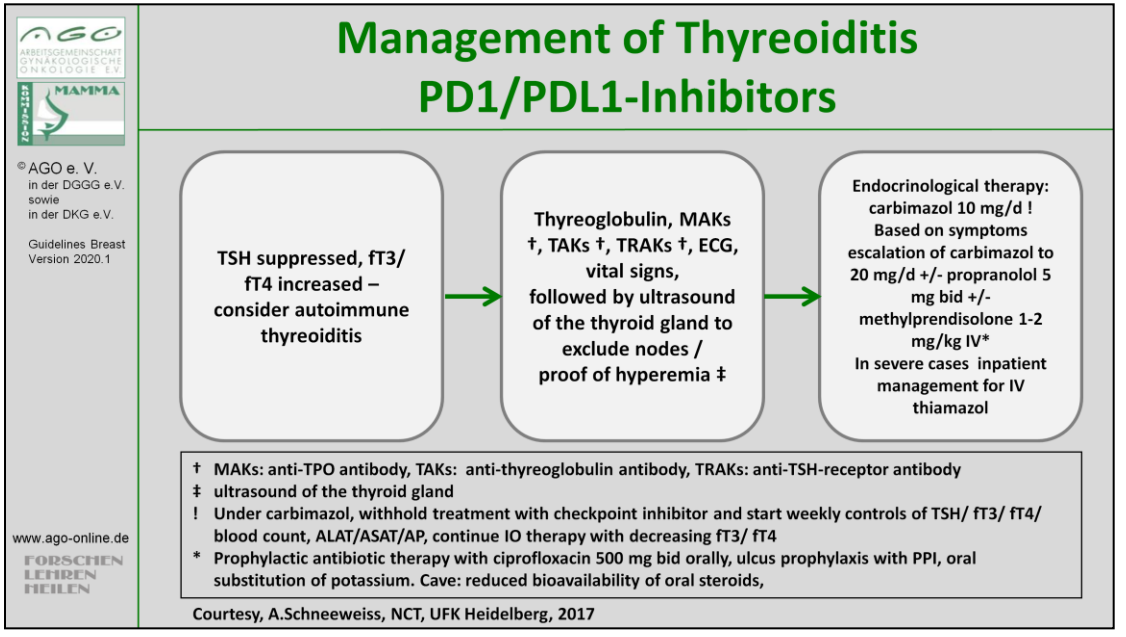

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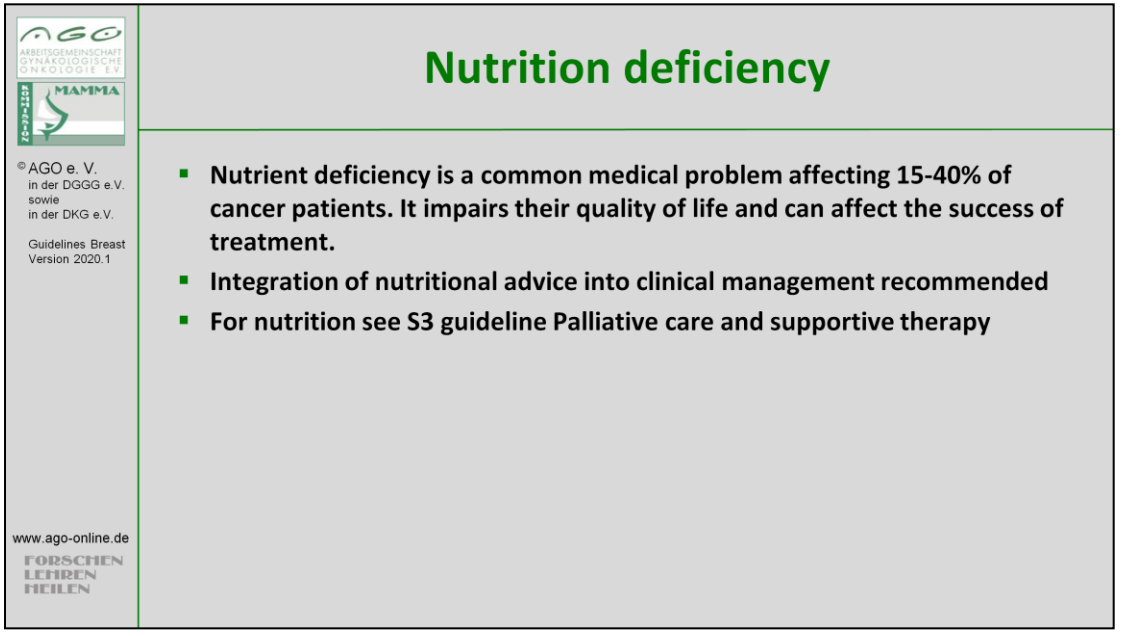
- **Further supportive and palliative issues**
  - **Nutrition**
  - **Pain management**
  - **Palliative Care**



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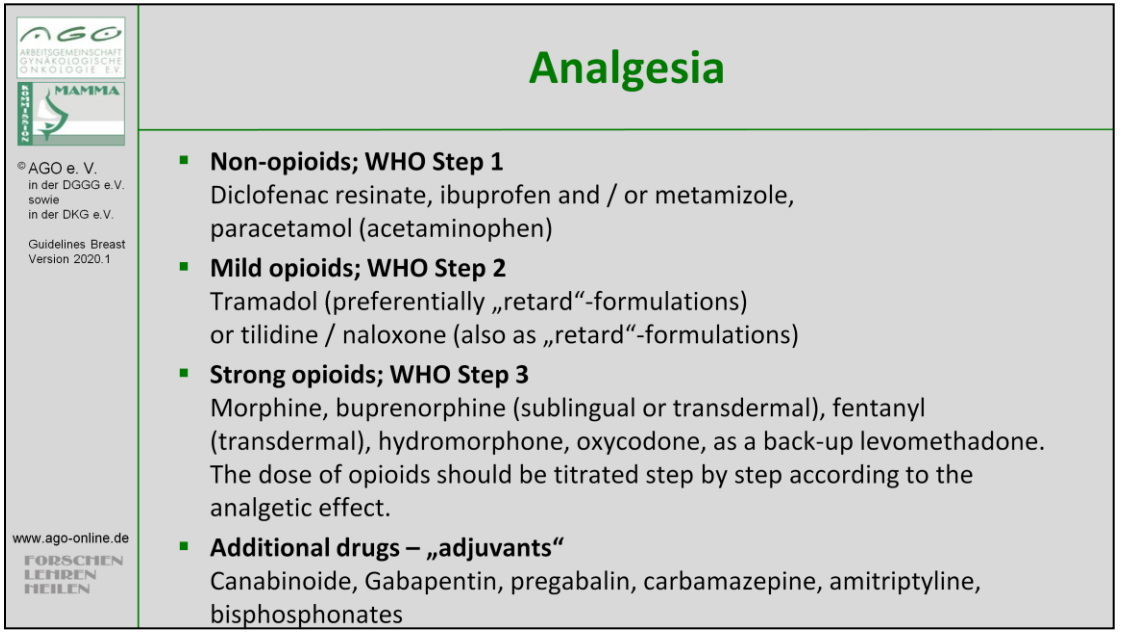

Relevant practice guideline:

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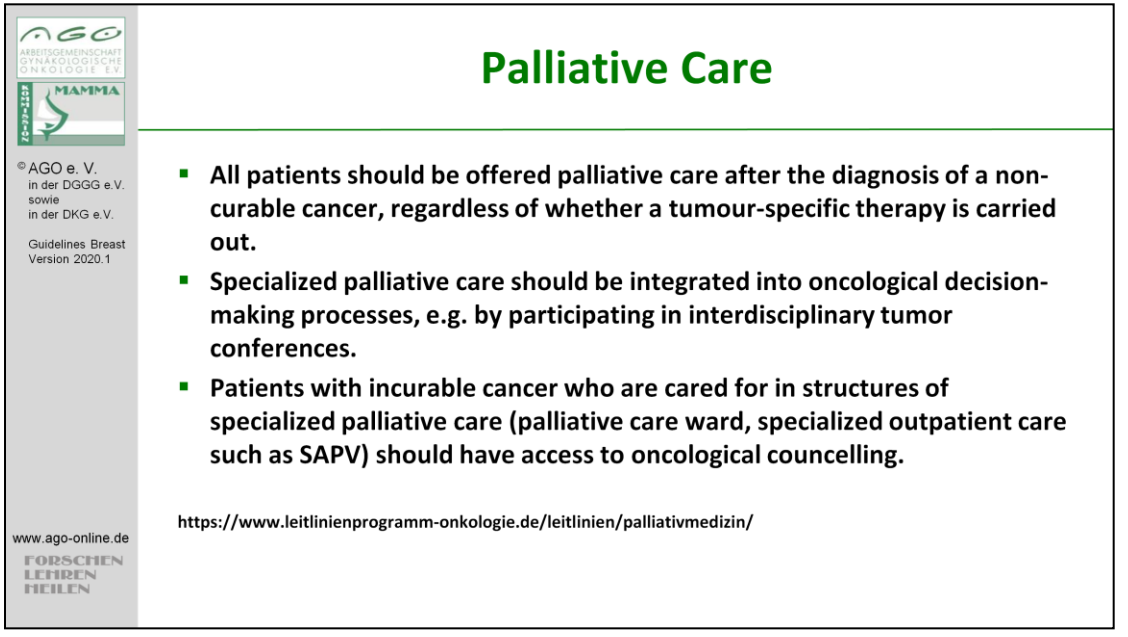
Relevant practice guideline:

2. Horlemann J, Schürmann N. DGS Praxisleitlinien in der Schmerztherapie. Canabis in der Schmerzmedizin v 1.0 www.dgs-praxisleitlinien.de/index.php/leitlinien/cannabis



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