Screened data bases

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

Screened guidelines

1. ABC Consensus Guidelines for Advanced Breast Cancer (ABC 1-4): Cardoso F, Costa A, Senkus E et al. 3rd ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 3). Ann Oncol. 2017 Jan 1;28(1):16-33.
2. Thomssen C. et al. ABC5 Consensus: assessment by a German Group of Experts. Breast Care (Basel). 2020
3. ASCO (American Association of Clinical Oncology, Practice Guidelines, 2019) http://www.asco.org
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
5. 2016 Updated American Society of Clinical Oncology/Oncology Nursing Society Chemotherapy Administration Safety Standards, Including Standards for Pediatric Oncology: http://ascopubs.org/doi/pdfdirect/10.1200/JOP.2016.017905
6. Hershman DL, Lacchetti C, Dworkin RH et al. American Society of Clinical Oncology. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014 Jun 20;32(18):1941-67.

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 Therapie und Nebenwirkungsmanagement

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- **Version 2002–2019:**
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- **Version 2020:**
  Müller / Albert

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Inhaltsverzeichnis

- Leitlinien
- Toxizitätsbeurteilung
- Inzidenz von Nebenwirkungen
  (nach Fachinformationen; MedDRA-Standard)
- Nebenwirkungen nach Organsystemen
  - Inzidenz, Prävention, Therapie
- Substanzspezifische Nebenwirkungen
  - Zielgerichtete Substanzen
- Andere Fragestellungen
  - Schmerztherapie, Palliative Care

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- **Leitlinien - Umfeld**

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

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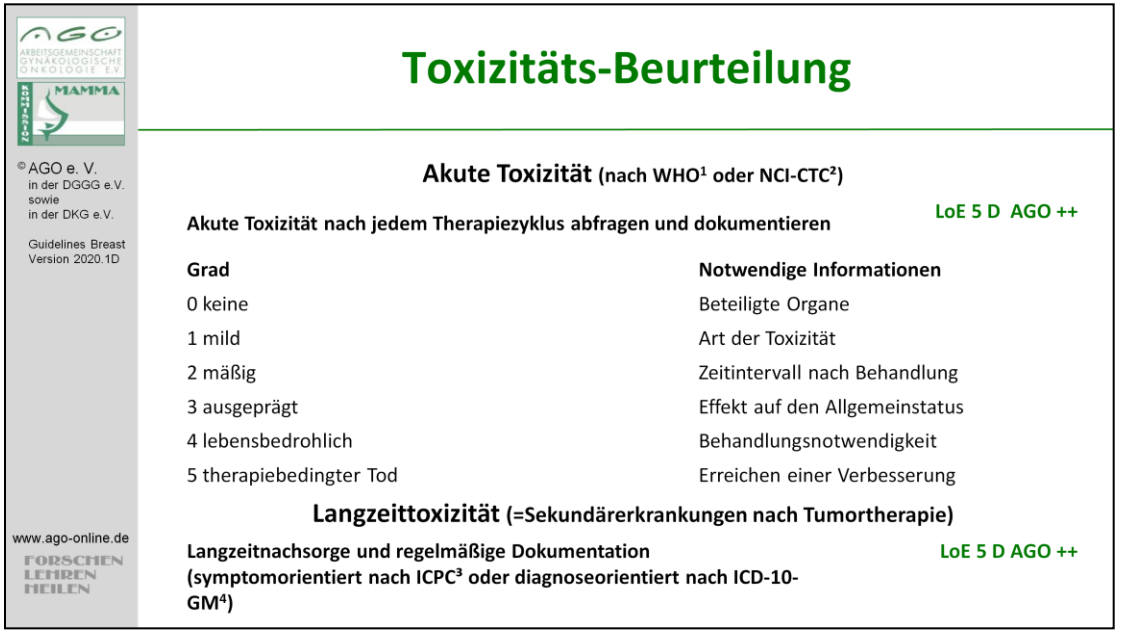
- **Toxizitätsbeurteilung**
  - **Akute Toxizität (NCI-CTCAE)**
  - **Langzeittoxizität (ICPC, ICD-GM)**



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)

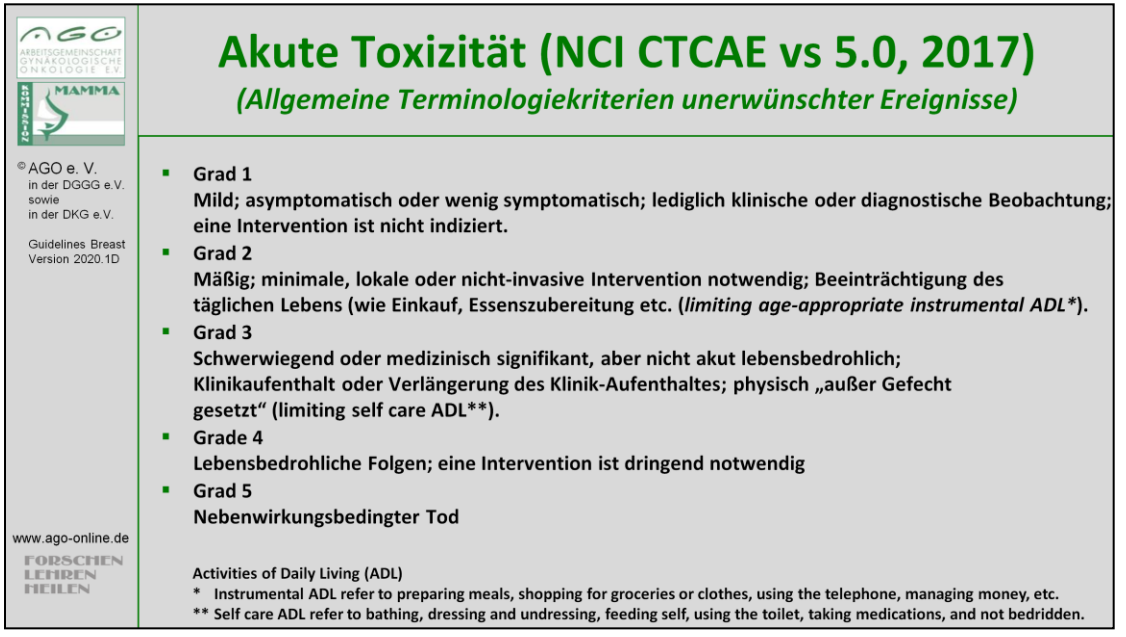
Akute Toxizität nach jedem Therapiezyklus abfragen

1. Cirillo M, Lunardi G, Coati F, et al: Management of oral anticancer drugs: Feasibility and patient approval of a specific monitoring program. Tumori 100: 243-248, 2014

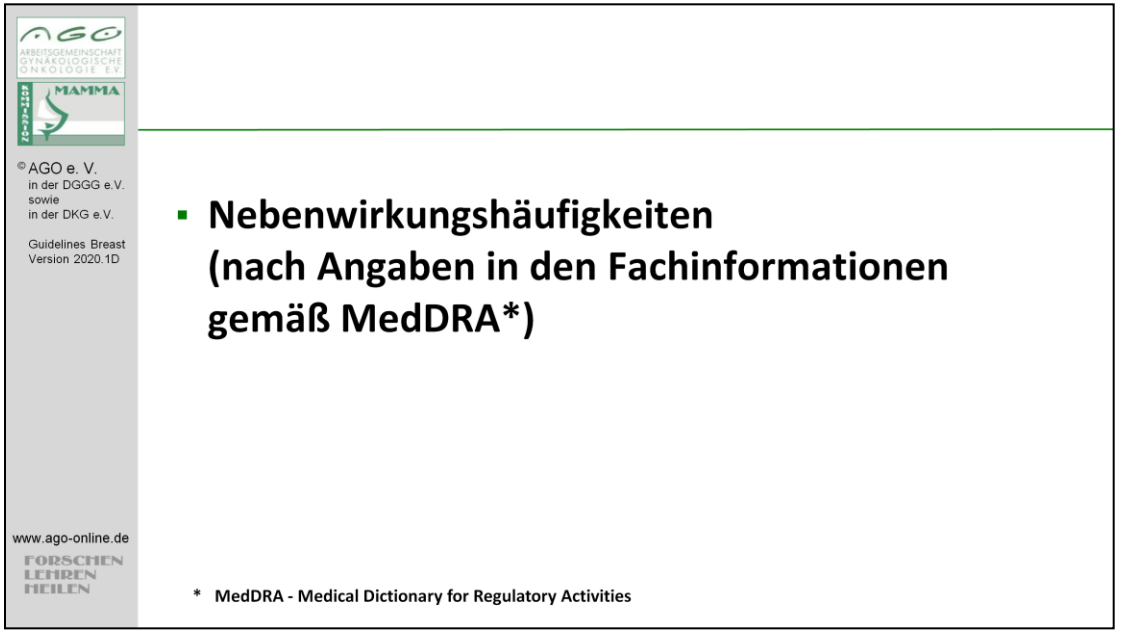
Langzeittoxizität

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)
3. Kenyon M, Mayer DK, Owens AK. Late and long-term effects of breast cancer treatment and surveillance management for the

general practitioner. J Obstet Gynecol Neonatal Nurs. 2014 May-Jun;43(3):382-98.
4. Hematopoietic Cell Transplantation Guidelines Taskforce, Auditory and Vision Guidelines Taskforce, Cardiopulmonary Guidelines Taskforce, Endocrine Guidelines Taskforce, Genitourinary and Renal Guidelines Taskforce, Oral, Dental, Gastrointestinal and Hepatic Guidelines Taskforce, et al. Late Effects Surveillance Recommendations among Survivors of Childhood Hematopoietic Cell Transplantation: A Children's Oncology Group Report. Author manuscript; available in PMC 2017 May 1.Published in final edited form as: Biol Blood Marrow Transplant. 2016 May; 22(5): 782–795.
5. Inge Spronk, Joke C Korevaar, Francois G Schellevis, et al. Evidence-based recommendations on care for breast cancer survivors for primary care providers: a review of evidence-based breast cancer guidelines. BMJ Open. 2017; 7(12): e015118.
6. M.J. Heins, J.C. Korevaar, P.M. Rijken, et al. For which health problems do cancer survivors visit their General Practitioner? European Journal of Cancer (2013) 49, 211– 218.

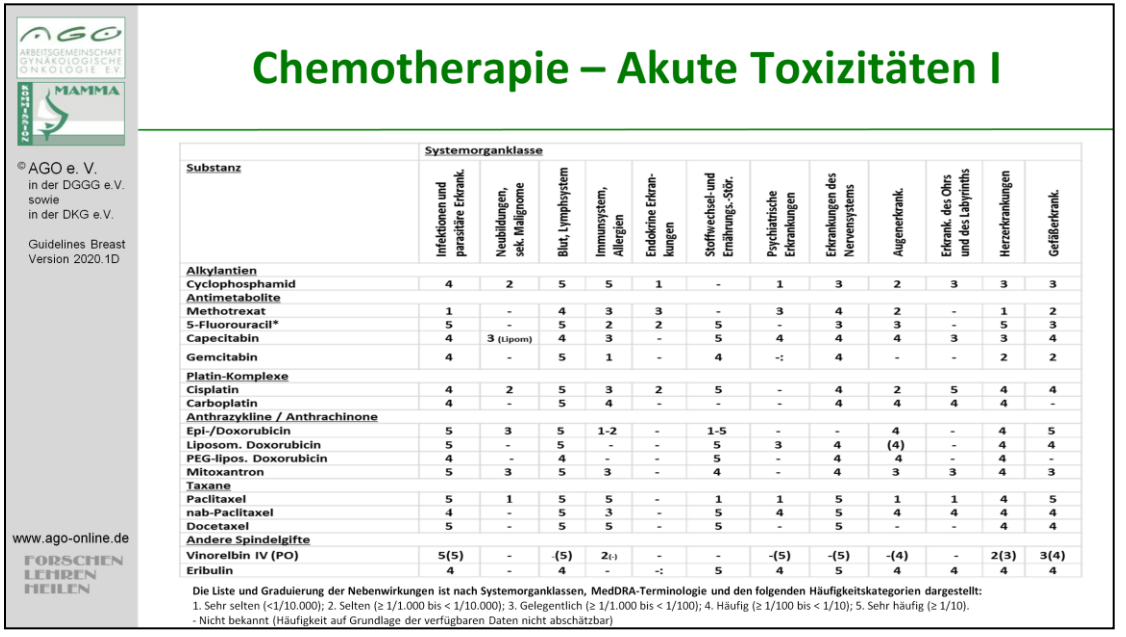


1. NCI, Bethesda, USA, Common Terminology Criteria for Adverse Events v5.0 (CTCAE; published 2017); https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50 (Download 18.01.2018)



*MedDRA - Medical Dictionary for Regulatory Activities

https://www.meddra.org/



Chemotherapie – Akute Toxizitäten I

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

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

Nebenwirkungskategorien - MedDRA (Medical Dictionary for Regulatory Activities)
MedDRA: https://www.meddra.org/ bzw.
https://www.meddra.org/sites/default/files/guidance/file/intguide_20_1_english_0.pdf

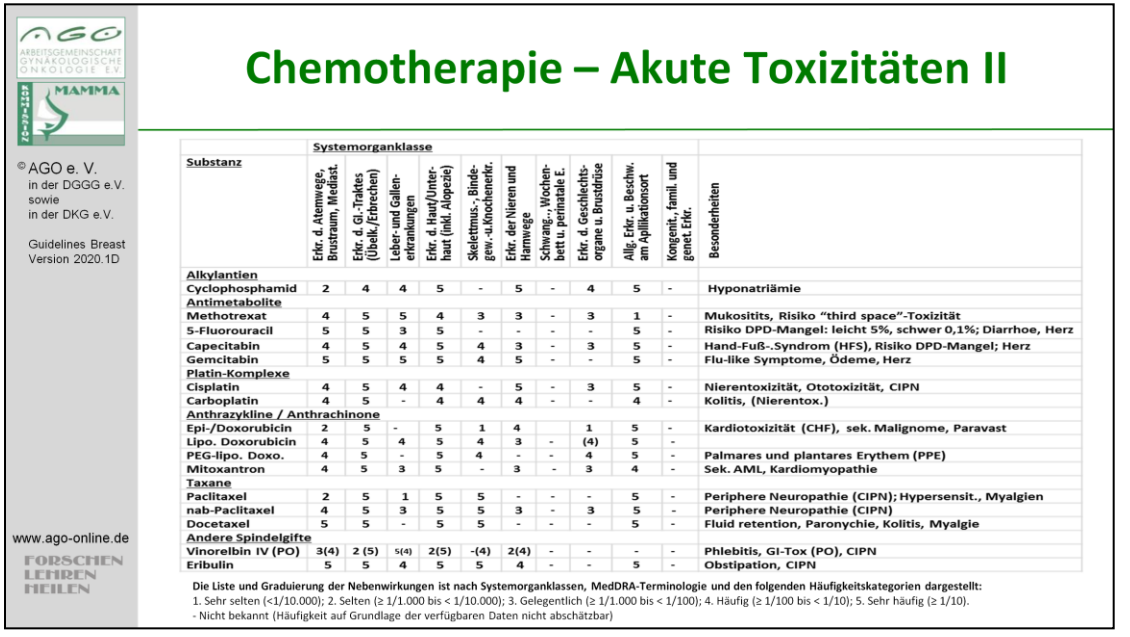
Quellen für die Fachinformationen (Download 19.01.2018)
Cyclophosphamid: http://www.baxter.de/de_DE/assets/downloads/fachinformation/endoxan.pdf
Methotrexat: https://www.gelbe-liste.de/produkte/MTX-HEXAL-10-mg-Tabletten_117469/fachinformation
5-Fluorouracil: https://www.gelbe-liste.de/produkte/Fluorouracil-HEXAL-50-mg-ml-Injektionsloesung-100-ml_546519/fachinformation
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

Weitere Referenzen (Auswahl)

1. Azim HA Jr, de Azambuja E, Colozza M, et al.: Long-term toxic effects of adjuvant chemotherapy in breast cancer. Ann Oncol. 2011 Sep;22(9):1939-47.
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
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.
7. Maeda S, Saimura M, Minami S, et al. Efficacy and safety of eribulin as first- to third-line treatment in patients with advanced or metastatic breast cancer previously treated with anthracyclines and taxanes.See comment in PubMed Commons below Breast. 2017 Jan 2;32:66-72. doi: 10.1016/j.breast.2016.12.017.
8. Zhang XH, Hao S, Gao B, et al. A network meta-analysis for toxicity of eight chemotherapy regimens in the treatment of metastatic/advanced breast cancer. Oncotarget. 2016 Dec 20;7(51):84533-84543. doi: 10.18632/oncotarget.13023.
9. Basch E, Prestrud AA, Hesketh PJ, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. Journal of Clinical Oncology 2011;29:4189- 4198
10. Crawford J.
11. NCCN, editor. NCCNR Practice Guidelines in Oncology - v.1.2011; Myeloid Growth Factors. National Comprehensive Cancer Network 2011. 18-7-2011.
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.



Chemotherapie – Akute Toxizitäten II

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

Die Liste und Graduierung der Nebenwirkungen ist nach Systemorganklassen, MedDRA-Terminologie und den folgenden Häufigkeitskategorien dargestellt:
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- Nicht bekannt (Häufigkeit auf Grundlage der verfügbaren Daten nicht abschätzbar)

Abkürzungen

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

Nebenwirkungskategorien - MedDRA (Medical Dictionary for Regulatory Activities)

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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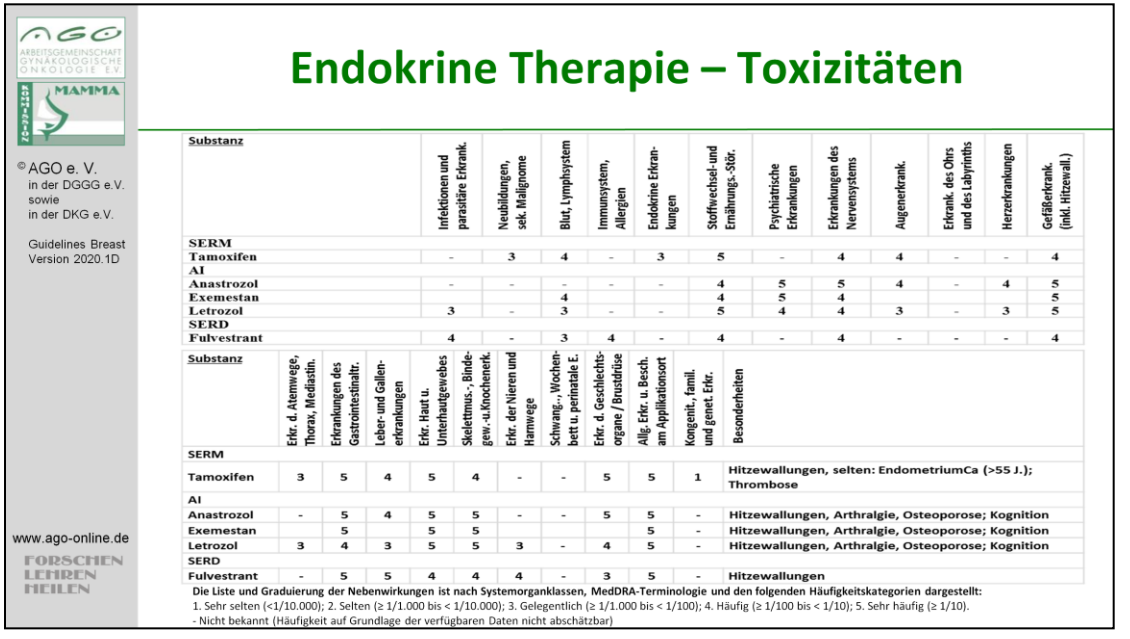
7. Maeda S, Saimura M, Minami S, et al. Efficacy and safety of eribulin as first- to third-line treatment in patients with advanced or metastatic breast cancer previously treated with anthracyclines and taxanes.See comment in PubMed Commons below Breast. 2017 Jan 2;32:66-72. doi: 10.1016/j.breast.2016.12.017.
8. Zhang XH, Hao S, Gao B, et al. A network meta-analysis for toxicity of eight chemotherapy regimens in the treatment of metastatic/advanced breast cancer. Oncotarget. 2016 Dec 20;7(51):84533-84543. doi: 10.18632/oncotarget.13023.
9. Basch E, Prestrud AA, Hesketh PJ, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. Journal of Clinical Oncology 2011;29:4189- 4198
10. Crawford J.
11. NCCN, editor. NCCNR Practice Guidelines in Oncology - v.1.2011; Myeloid Growth Factors. National Comprehensive Cancer Network 2011. 18-7-2011.
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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LEHREN
HEILEN

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

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

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

<u>Nebenwirkungskategorien - MedDRA (Medical Dictionary for Regulatory Activities)</u>
MedDRA: https://www.meddra.org/ bzw.
https://www.meddra.org/sites/default/files/guidance/file/intguide_20_1_english_0.pdf

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

Nebenwirkungen nach Organsystemen
Inzidenz, Prävention, Therapie

1. Infektionen u. parasitäre Erkrankungen

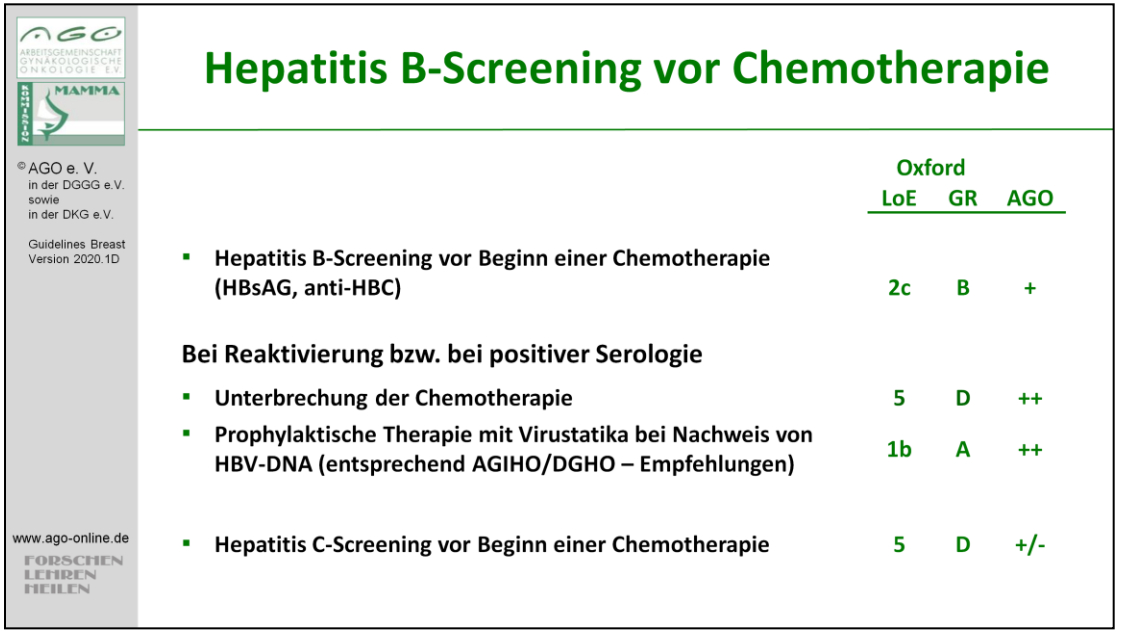
- Allgemeine Infektionsprophylaxe
- Hepatitis B-Screening

ASCO:

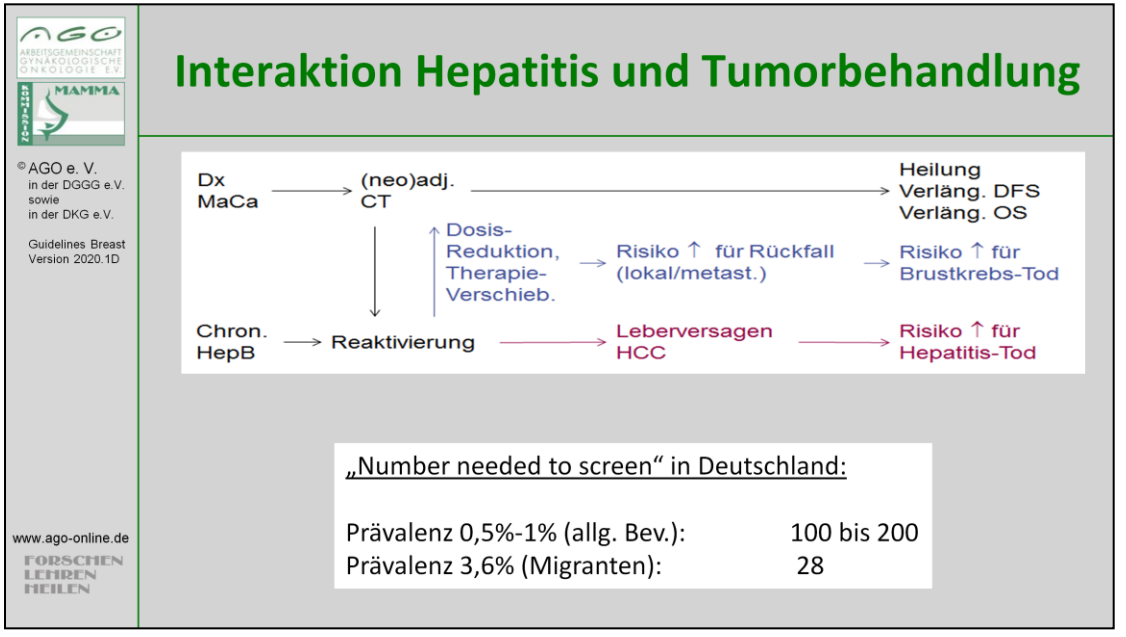
Taplitz RA, Kennedy EB, Bow EJ, Crews J, Gleason C, Hawley DK, Langston AA, Nastoupil LJ, Rajotte M, Rolston K, Strasfeld L, Flowers CR: Outpatient management of fever and neutropenia in adults treated for malignancy: American society of clinical oncology and infectious diseases society of america clinical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

NCCN:

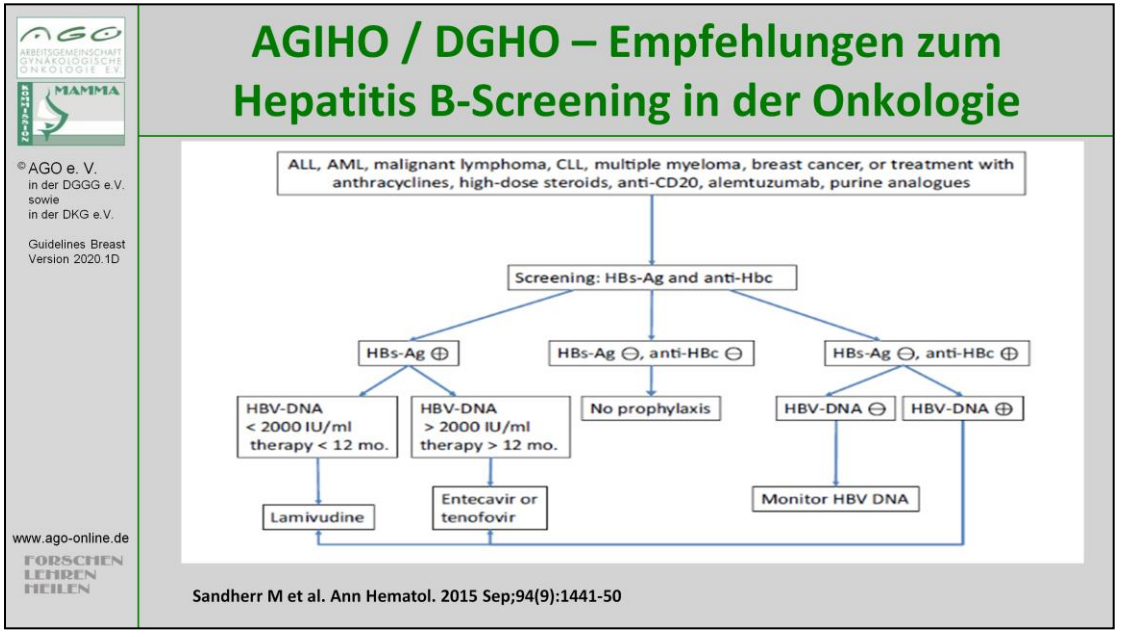
NCCN Guidelines Version 1.2020 Prevention and Treatment of Cancer-Related Infections.
https://www.nccn.org/professionals/physician_gls/PDF/infections.pdf



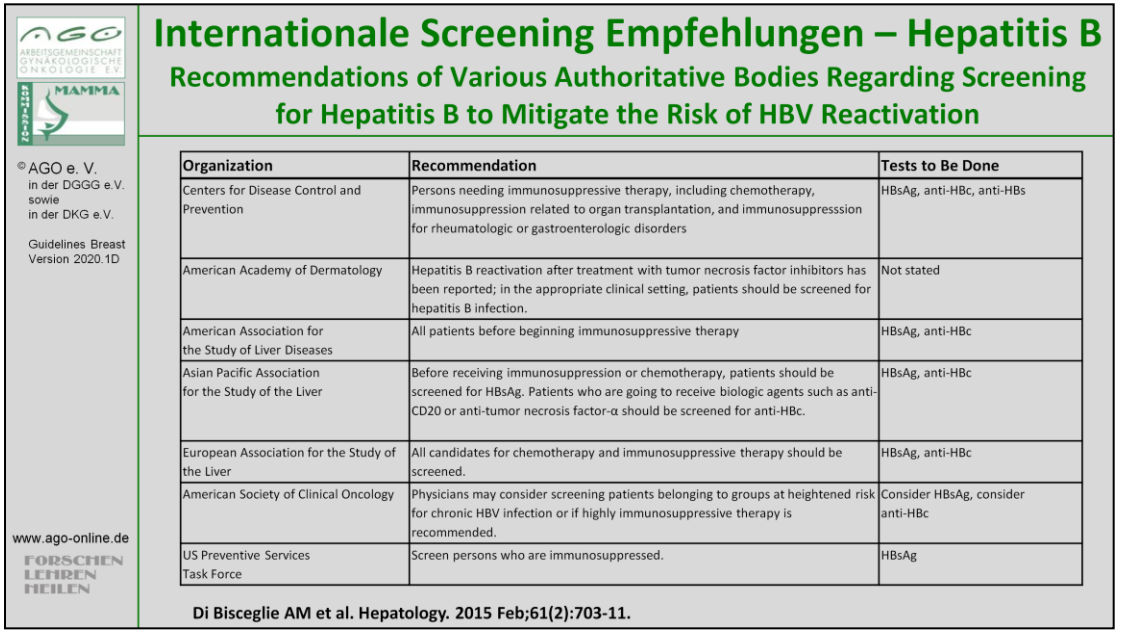
1. Sandherr M, Hentrich M, von Lilienfeld-Toal M, et al. Antiviral prophylaxis in patients with solid tumours and haematological malignancies--update of the Guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society for Hematology and Medical Oncology (DGHO). Ann Hematol. 2015 Sep;94(9):1441-50.
2. Robert-Koch-Institut. Epidemiologisches Bulletin. 20. Juli 2015 / Nr. 29
3. Di Bisceglie AM, Lok AS, Martin P, et al. Recent US Food and Drug Administration warnings on hepatitis B reactivation with immune-suppressing and anticancer drugs: just the tip of the iceberg? Hepatology. 2015 Feb;61(2):703-11.
4. Liu Z, Jiang L, Liang G, et al. Hepatitis B virus reactivation in breast cancer patients undergoing chemotherapy: A review and meta-analysis of prophylaxis management. J Viral Hepat. 2017 Jan 10.
5. Levaggi A, De Maria A, Dozin B, et al. Incidence of hepatitis in patients with evidence of past or current hepatitis B or C during chemotherapy for early breast cancer. Anticancer Res. 2014 Jul;34(7):3715-20.
6. NCCN Guidelines Version 1.2018: Prevention and Treatment of Cancer-Related Infections. https://www.nccn.org/professionals/physician_gls/pdf/infections.pdf



1. Wong WW, Hicks LK, Tu HA et al. Hepatitis B virus screening before adjuvant chemotherapy in patients with early-stage breast cancer: a cost-effectiveness analysis. Breast Cancer Res Treat. 2015 Jun;151(3):639-52.



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.
2. Maschmeyer G, De Greef J, Mellinghoff SC, Nosari A, Thiebaut-Bertrand A, Bergeron A, Franquet T, Blijlevens NMA, Maertens JA, European Conference on Infections in L: Infections associated with immunotherapeutic and molecular targeted agents in hematology and oncology. A position paper by the european conference on infections in leukemia (ecil). Leukemia 2019;33:844-862.



1. Di Bisceglie AM, Lok AS, Martin P, et al. Recent US Food and Drug Administration warnings on hepatitis B reactivation with immune-suppressing and anticancer drugs: just the tip of the iceberg? Hepatology. 2015 Feb;61(2):703-11.
2. https://www.asco.org/practice-guidelines/quality-guidelines/guidelines/supportive-care-and-treatment-related-issues#/9811
3. European Association For The Study Of The Liver. EASL clinical practice guidelines: Management of chronic hepatitis B virus infection. J Hepatol. 2012 Jul;57(1):167-85.
4. European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol. 2017 Aug;67(2):370-398.

Nebenwirkungen nach Organsystemen
Inzidenz, Prävention, Therapie

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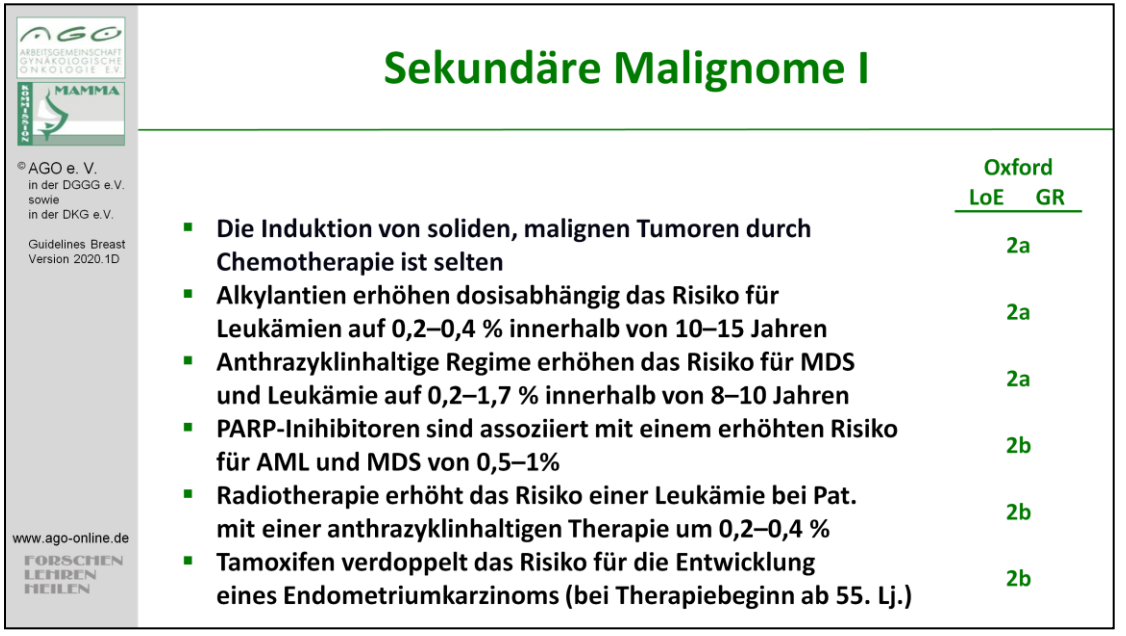
2. Gutartige, bösartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen)



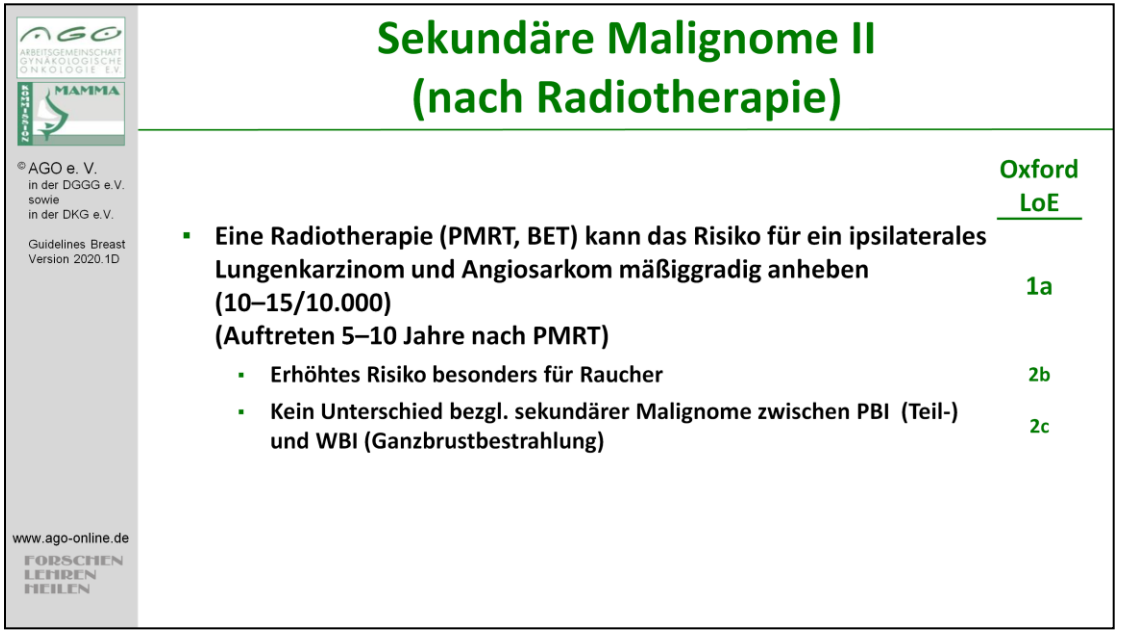
Statements 1-4

1. Schaapveld M, Visser O, Louweman M et al.(2008) Risk of primary non breast cancers after breast cancer treatment: a dutch population-based study. J Clin Oncol 26: 1239-46.
2. Kirova Y, De Rycke Y, Gambotti L et al.(2008) Second malignancies after breast cancer: the impact of different treatment modalities. B J Cancer 98: 870-4.
3. Andersson M, Jensen M, Engholm G, et al (2008) Risk of secondary primary cancer among patients with early operable breast cancer registered or randomised in Danish Breast Cancer cooperative Group (DBCG) protocols of the 77, 82, 89 programmes during 1977-2001. Ann Oncol 47: 755-64.
4. Beadle G, Baade P, Fritschi L(2009) Acute myeloid leukemia after breast cancer: a population-based comparison with hematological malignancies and other cancers. Ann Oncol 20: 103-9.
5. Hershman D, Neugut A, Jacobson J et al.(2007) Acute myeloid leukemia or myelodysplastic syndrome following use of granulocyte colony-stmulating factors during breast cancer adjuvant chemotherapy. J Natl Cancer Inst 99: 196-205
6. Jabagi MJ, Goncalves A, Vey N, et al.: Risk of hematologic malignant neoplasms after postoperative treatment of breast cancer. Cancers (Basel) 2019;11.
7. Bazire L, De Rycke Y, Asselain B, et al. Risks of second malignancies after breast cancer treatment: Long-term results. Cancer Radiother. 2016 Dec 26. pii: S1278-3218(16)30478-4. doi:10.1016/j.canrad.2016.07.101. [Epub ahead of print]

8. Grantzau T, Overgaard J. Risk of second non-breast cancer among patients treated with and without postoperative radiotherapy for primary breast cancer: A systematic review and meta-analysis of population-based studies including 522,739 patients. Radiother Oncol. 2016 Dec;121(3):402-413. doi: 10.1016/j.radonc.2016.08.017. Epub 2016 Sep 14.
9. Jabagi MJ, Vey N, Goncalves A, et al.: Evaluation of the incidence of hematologic malignant neoplasms among breast cancer survivors in france. JAMA network open 2019;2:e187147.
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.
11. Jabagi MJ, Goncalves A, Vey N, et al.:Risk of hematologic malignant neoplasms after postoperative treatment of breast cancer. Cancers (Basel) 2019;11.

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.
2. Rosell J, Nordenskjöld B, Bengtsson NO, et al. Long-term effects on the incidence of second primary cancers in a randomized trial of two and five years of adjuvant tamoxifen. Acta Oncol. 2017 Jan 12:1-4. doi: 10.1080/0284186X.2016.1273547.
3. Dominick S, Hickey M, Chin J, et al.Levonorgestrel intrauterine system for endometrial protection in women with breast cancer on adjuvant tamoxifen. Cochrane Database Syst Rev. 2015 Dec 9;(12):CD007245. doi: 10.1002/14651858.CD007245.pub3.



1. Schaapveld M, Visser O, Louweman M et al.(2008) Risk of primary non-breast cancers after breast cancer treatment: a dutch population-based study. J Clin Oncol 26: 1239-46.
2. Berrington de Gonzalez A, Curtis R, Gilbert E et al.(2010) Second solid cancers after radiotherapy for breast cancer in SEER cancer registries. B J Cancer 102: 220-6.
3. EBCTCG (2005) Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15 year survival: an overview of randomised trials. Lancet 366: 2087-3106.
4. Senkus-Konefka E, Jassem J(2011) Complications of Breast cancer Radiotherapy. J Clin Oncol 18: 229-35.
5. Kaufman E, Jacobson J, Hershman D, et al.(2008) Effect of breast cancer radiotherapy and cigarette smoking on risk of secundary lung cancer. J Clin Oncol 26: 392-8.
6. Kirova Y, De Rycke Y, Gambotti L et al.(2008) Second malignancies after breast cancer: the impact of different treatment modalities. B J Cancer 98: 870-4.
7. Le Deley M, Suzan F, Catali B et al.(2007) Anthracyclines, mitroxantrone, radiotherapy, and granulocyte colony-stimulating factor: risik factors for leukemia and myelodsplastic syndrome after breast cancer. J Clin Oncol 25: 292-300.
8. Smith R(2003) Risk for the development of treatment-related acute myelocytic leukemia and myelodysplastic syndrome: review of the literature and the National Surgical Adjuvant Breast and Bowel Projekt Experience. Clin Breast Cancer 4: 273-9
9. Santos AM, Marcu LG, Wong CM, et al. Risk estimation of second primary cancers after breast radiotherapy. Acta Oncol. 2016

Nov;55(11):1331-1337. Epub 2016 Jul 5.
10. Pan XB, Huang ST, Jiang YM, et al. Secondary malignancies after partial versus whole breast irradiation: a systematic review and meta-analysis. Oncotarget. 2016 Nov 1;7(44):71951-71959. doi: 10.18632/oncotarget.12442.
11. Takahashi S, Murakami Y, Imano N, et al. Long-term results after 12-year follow-up of patients treated with whole-breast and boost irradiation after breast-conserving surgery. Jpn J Radiol. 2016 Sep;34(9):595-604. doi: 10.1007/s11604-016-0562-2. Epub 2016 Jun 17.
12. Sheth GR et al (2012) Radiation-induced sarcoma of the breast: a systematic review. Oncologist 17(3) 405–18 DOI: 10.1634/theoncologist.2011-0282 PMID: 22334455 PMCID: 3316927

Guidelines Breast
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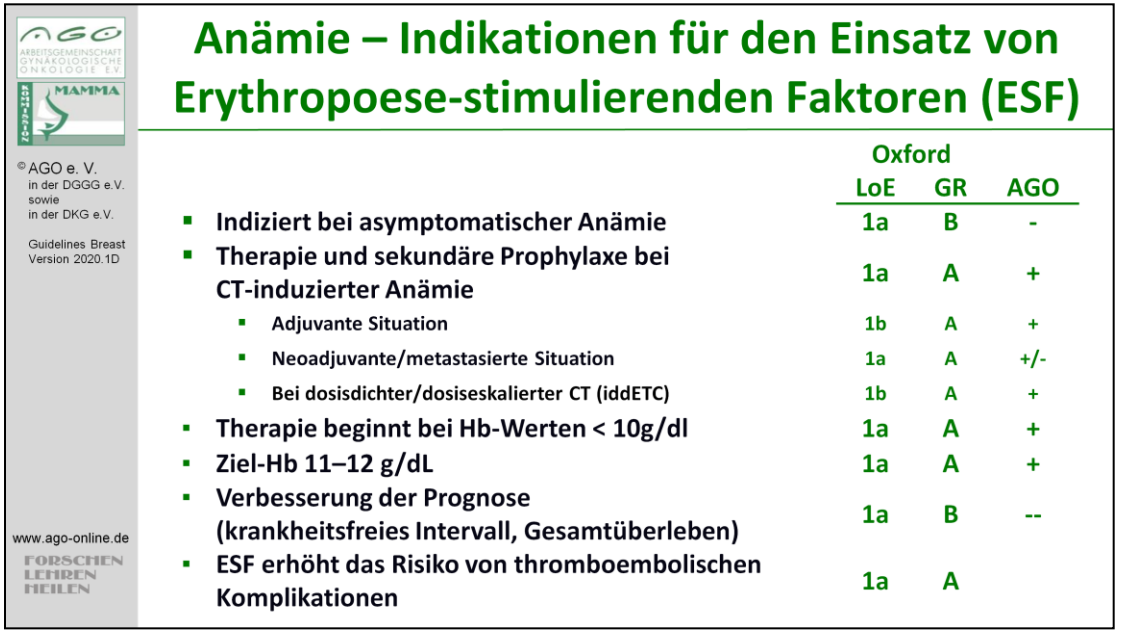
Nebenwirkungen nach Organsystemen
Inzidenz, Prävention, Therapie

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



Leitlinie:

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. Bohlius J, Bohlke K, Castelli R, et al: Management of cancer-associated anemia with erythropoiesis-stimulating agents: Asco/ash clinical practice guideline update. J Clin Oncol 2019;37:1336-1351.

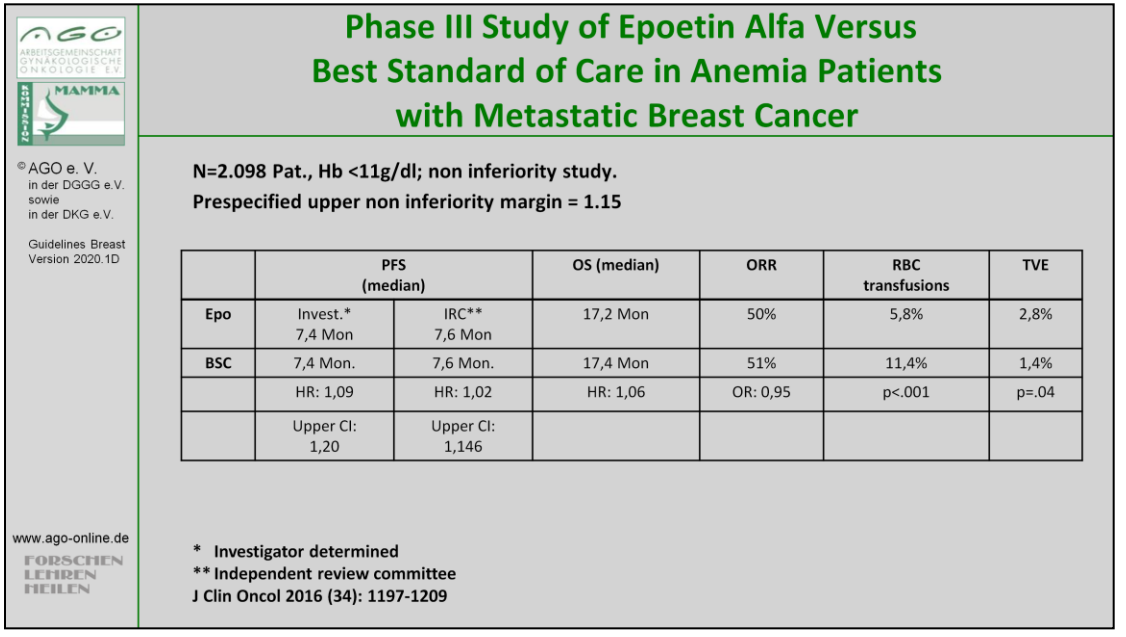
2. Mountzios G, Aravantinos G, Alexopoulou Z et al.: Lessons from the past: Long-term safety and survival outcomes of a prematurely terminated randomized controlled trial on prophylactic vs. Hemoglobin-based administration of erythropoiesis-stimulating agents in patients with chemotherapy-induced anemia. Molecular and clinical oncology 4: 211-220, 2016.
3. Leyland-Jones B, Bondarenko I, Nemsadze G et al.: A randomized, open-label, multicenter, Phase III study of epoetin alfa versus best standard of care in anemic patients with metastatic breast cancer receiving standard chemotherapy. J Clin Oncol 34: 1197-

1207, 2016.
4. Lai Y, Ye Z, Civan JM et al.: The effects of erythropoiesis-stimulating agents on the short-term and long-term survivals in metastatic breast cancer patients receiving chemotherapy: a SEER population-based study. Breast Cancer Res Treat 153: 407-416, 2015.
5. Aapro M, Moebus V, Nitz U et al.: Safety and efficacy outcomes with erythropoiesis-stimulating agents in patients with breast cancer: a meta-analysis. Annals of Oncology 26: 688-695, 2015.
6. Lai Y, Palazzo JP, Cristofanilli M et al.: Erythropoiesis stimulating agents and clinical outcomes of invasive breast cancer patients receiving cytotoxic chemotherapy. Breast Cancer Res Treat 148: 175-185, 2014.
7. Moebus V, Jackisch C, Schneeweiss A et al.: Adding epoetin alfa to intense dose-dense adjuvant chemotherapy for breast cancer. Randomized clinical trial. J Natl Cancer Inst; 2013; 105: 1018-1026.
8. Swain SM, Tang G, Geyer CE Jr, et al. Definitive Results of a Phase III Adjuvant Trial Comparing Three Chemotherapy Regimens in Women With Operable, Node-Positive Breast Cancer: The NSABP B-38 Trial. J Clin Oncol 2013; 31: 3197-3204.
9. Untch M, Fasching PA, Konecny GE, et al. PREPARE trial: a randomized phase III trial comparing preoperative, dose-dense, dose-intensified chemotherapy with epirubicin, paclitaxel and CMF versus a standard dosed epirubicin/cyclophosphamide followed by paclitaxel ± darbepoetin alfa in primary breast cancer—results at the time of surgery. Ann Oncol. 2011;22:1988–1998.
10. Nitz U, Gluz O, Oberhoff C, et al. Adjuvant chemotherapy with or without darbepoetin alpha in node-positive breast cancer: survival and quality of life analysis from the prospective randomized WSG ARA Plus trial. Cancer Res. 2011;71(24 suppl):143s.
11. Glaspy J, Crawford J, Vansteenkiste J, et al. Erythropoiesis-stimulating agents in oncology: a study-level meta-analysis of survival and other safety outcomes. Br J Cancer. 2010;102:301–315.
12. Bohlius J, Schmidlin K, Brillant C, et al. Recombinant human erythropoiesis-stimulating agents and mortality in patients with cancer: a metaanalysis of randomised trials. Lancet 2009;374:28.
13. Crouch Z, DeSantis ER. :Use of erythropoietin-stimulating agents in breast cancer patients: a risk review. Am J Health Syst Pharm. 2009 Jul 1;66(13):1180-5.
14. Hershman DL, Buono DL, Malin J, et al.: Patterns of use and risks associated with erythropoiesis-stimulating agents among Medicare patients with cancer. J Natl Cancer Inst. 2009 Dec 2;101(23):1633-41.
15. Manzoni M, Delfanti S, Rovati B, et al.: Chemotherapy-induced anemia in breast cancer patients treated with pegfilgrastim-supported dose-dense regimens. Clin Exp Med. 2009 Oct 10. [Epub ahead of print]PMID: 19821012 [PubMed - as supplied by publisher]
16. Miller CP, Lowe KA, Valliant-Saunders K, et al.: Evaluating erythropoietin-associated tumor progression using archival tissues from a phase III clinical trial. Stem Cells. 2009 Sep;27(9):2353-61.

17. Bohlius J, Schmidlin K, Brillant C, et al. Recombinant human erythropoiesis stimulating agents and mortality in patients with cancer: a meta-analysis of randomized trials. Lancet. 2009;373:1532–1542.
18. Tonelli M; Hemmalgarn B, Reimann T, et al. Benefits and harms of erythropoiesis-stimulating agents for anemia related to cancer. A meta-analysis. CMAJ. 2009;180:E62–E71
19. Ludwig H, Crawford J, Osterborg A, et al. Pooled analysis of individual patient-level data from all randomized, double-blind, placebo-controlled trials of darbepoetin alfa in the treatment of patients with chemotherapy induced anemia. J Clin Oncol. 2009;27:2838–2847
20. Bennett CL, Silver SM, Djulbegovic B, et al. Venous thromboembolism and mortality associated with recombinant erythropoietin and darbepoetin administration for the treatment of cancer-associated anemia. JAMA. 2008;299:914–924.
21. Leyland-Jones B, Semiglazov V, Pawlicki M, et al. Maintaining normal hemoglobin levels with epoetin alfa in mainly nonanemic patients with metastatic breast cancer receiving first-line chemotherapy: a survival study. J Clin Oncol. 2005;23:5960–5972.

Relevante Leitlinien

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)
2. Rodgers GM, Gilreath JA et al: Cancer- and chemotherapy-induced anemia. NCCN Clinical Practice Guidelines in Oncology 2.2015. Available from: URL: http://www.nccn.org
3. Rizzo JD et al: ASCO/ASH/Clinical Practice Guideline update on the use of epoetin and darbepoetin in adult patients with cancer. J Clin Oncol 2010; 28: 4996–10
4. Aapro MS, Link H. September 2007 update on EORTC guidelines and anemia management with erythropoiesis-stimulating agents. Oncologist 2008;13(Suppl):33–36.
5. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.1, 2017, AWMF Registernummer: 032/054OL, http://leitlinienprogramm-onkologie.de/Supportive-Therapie.95.0.html (Zugriff 29. Januar 2018)



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

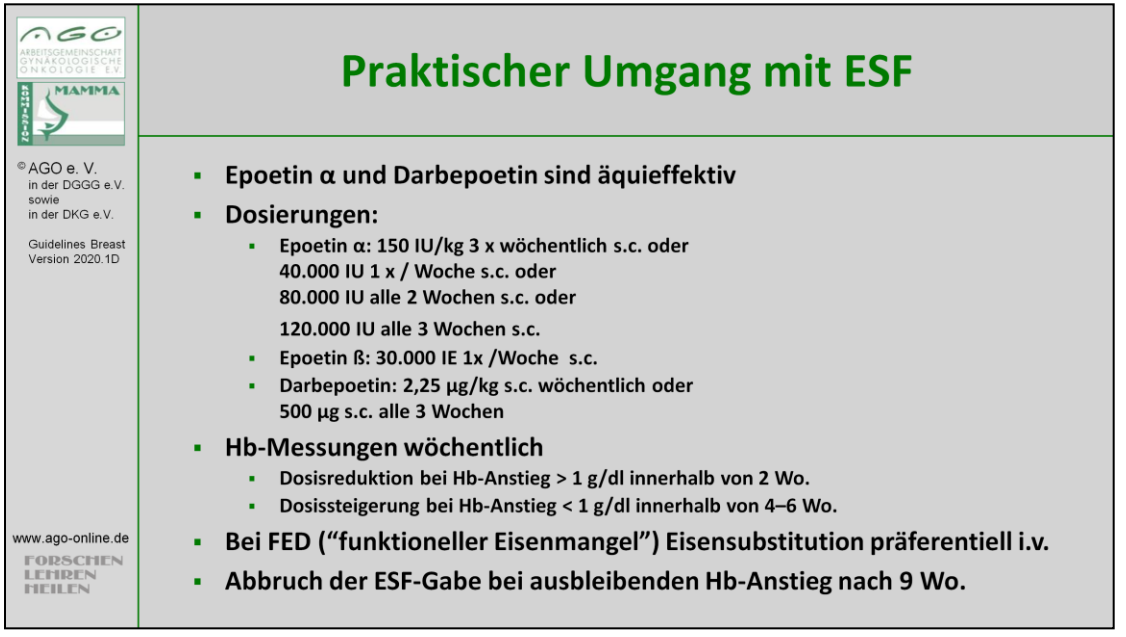
	PFS (median)		OS (median)	ORR	RBC transfusions	TVE
Epo	Invest.* 7,4 Mon	IRC** 7,6 Mon	17,2 Mon	50%	5,8%	2,8%
BSC	7,4 Mon.	7,6 Mon.	17,4 Mon	51%	11,4%	1,4%
	HR: 1,09	HR: 1,02	HR: 1,06	OR: 0,95	p<.001	p=.04
	Upper CI: 1,20	Upper CI: 1,146				

*** 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



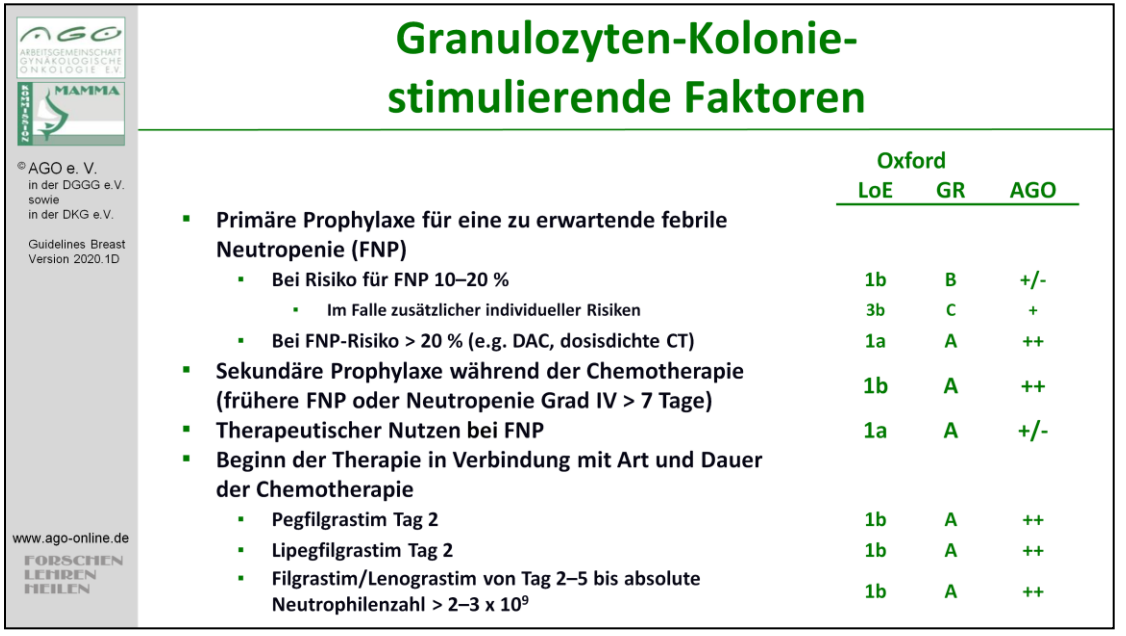
1. Bohlius J, Bohlke K, Castelli R, Djulbegovic B, Lustberg MB, Martino M, Mountzios G, Peswani N, Porter L, Tanaka TN, Trifiro G, Yang H, Lazo-Langner A: Management of cancer-associated anemia with erythropoiesis-stimulating agents: Asco/ash clinical practice guideline update. J Clin Oncol 2019;37:1336-1351.
2. Steensma DP, Sloan JA, Dakhil SR et al.: Phase III, Randomized study of the effects of parenteral iron, oral iron, or no iron supplementation on the erythropoietic response to darbepoetin alfa for patients with chemotherapy-associated anemia. J Clin Oncol 29: 97-105, 2010.
3. Pedrazzoli P, Farris A, Del Prete S et al.: Randomized trial of intravenous iron supplementation in patients with chemotherapy-related anemia without iron deficiency treated with darbepoetin alfa. J Clin Oncol 26: 1619-1625, 2008.
4. Bastit L, Vandebroek A, Altintas S et al.: Randomized, multicenter, controlled trial comparing the efficacy and safetry of darbepoetin alfa administered every 3 weeks with or without intravenous iron in patients with chemotherapy-induced anemia. J Clin Oncol 26: 1611-1618, 2008.
5. Auerbach M, Ballard H, Trout JR et al.: Intravenous iron optimizes the response to recombinant human erythropoietin in cancer patients with chemotherapy-related anemia: A multicenter, open-label, randomized trial. J Clin Oncol 22: 1301-1307, 2004.

<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)
2. Rodgers GM, Gilreath JA et al: Cancer- and chemotherapy-induced anemia. NCCN Clinical Practice Guidelines in Oncology 2.2015. Available from: URL: http://www.nccn.org
3. Rizzo JD et al: ASCO/ASH/Clinical Practice Guideline update on the use of epoetin and darbepoetin in adult patients with cancer. J Clin Oncol 2010; 28: 4996–10
4. Aapro MS, Link H. September 2007 update on EORTC guidelines and anemia management with erythropoiesis-stimulating agents. Oncologist 2008;13(Suppl):33–36.
5. 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)



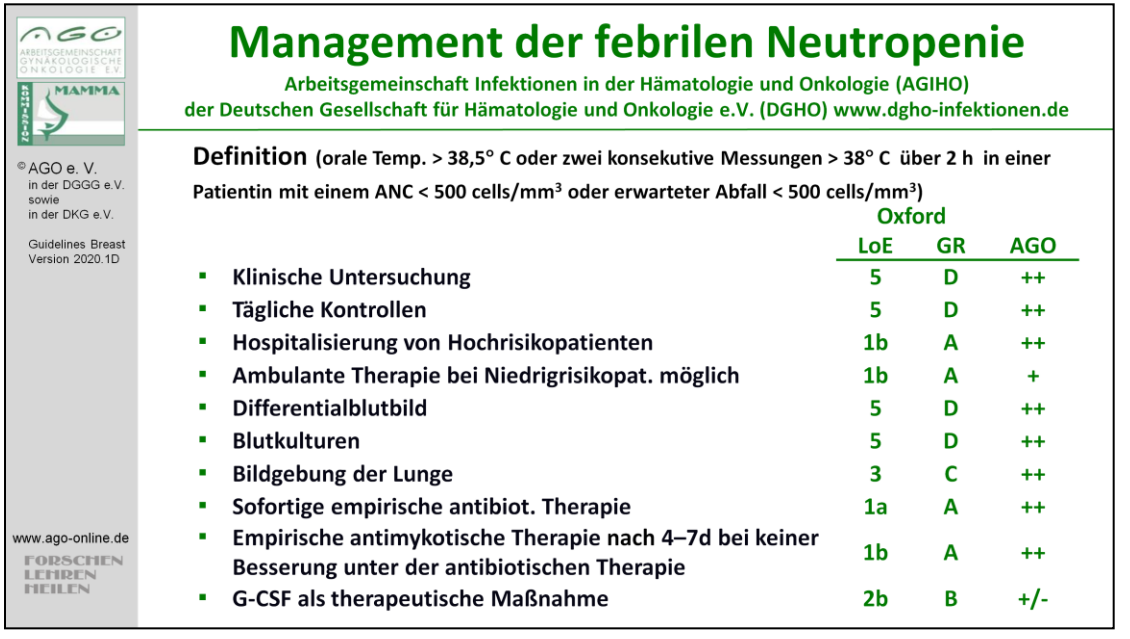
Relevante Leitlinien

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
2. NCCN Guidelines 2020
3. Smith TJ, Bohlke K, Lyman GH, et al.: American Society of Clinical Oncology. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2015 Oct 1;33(28):3199-212.

Statements 1-4

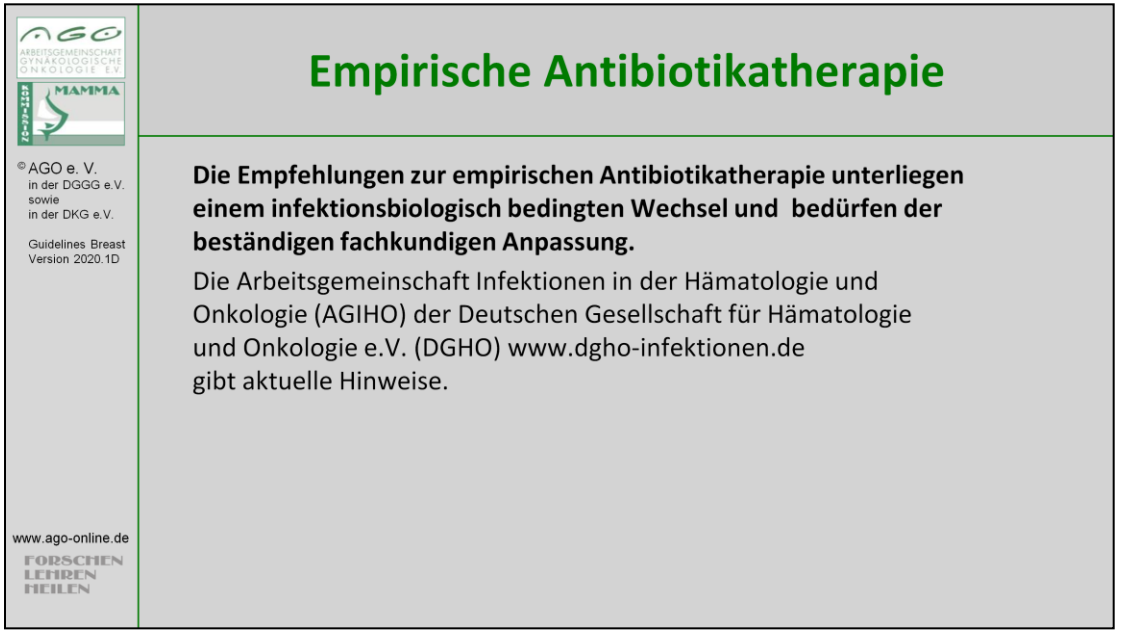
1. Bondarenko I, Gladkov OA, Elsaesser R et al.: Efficacy and safety of lipegfilgrastim versus pegfilgrastim: a randomized, multicenter, active-control phase 3 trial in patients with breast cancer receiving doxorubicin/docetaxel chemotherapy. BMC Cancer 2013, 13:386.
2. Lyman GH, Dale DC, Culakova E et al.: The impact of the granulocyte colony-stimulating factor on chemotherapy dose intensity and cancer survival: a systematic review and meta-analysis of randomized controlled trials. Ann Oncol 2013, 24: 2475-2484.
3. Loibl S, Mueller V, von Minckwitz G et al.: Comparison of pegfilgrastim on day 2 vs. day 4 as primary prophylaxis of intense dose-

dense chemotherapy in patients with node-positive primary breast cancer within the prospective, multi-center GAIN study: (GBG 33).Support Care Cancer. 2011, 19:1789-95.
4. Manzoni M, Delfanti S, Rovati B, et al.: Chemotherapy-induced neutropenia in breast cancer patients treated with pegfilgrastim-supported dose-dense regimens. Clin Exp Med. 2010 Jun;10(2):135-8.
5. Eubank TD, Roberts RD, Khan M, et al. Granulocyte macrophage colony-stimulating factor inhibits breast cancer growth and metastasis by invoking an anti-angiogenic program in tumor-educated macrophages. Cancer Res. 2009 Mar 1;69(5):2133-40.
6. Khan S, Dhadda A, Fyfe D, et al.: Impact of neutropenia on delivering planned chemotherapy for solid tumours. Eur J Cancer Care (Engl). 2008 Jan;17(1):19-25.
7. Arnedos M, Sutherland S, Ashley S, et al.: Routine prophylactic granulocyte colony stimulating factor (GCSF) is not necessary with accelerated (dose dense) paclitaxel for early breast cancer. Breast Cancer Res Treat. 2008 Nov;112(1):1-4.
8. Fontanella C, Bolzonello S, Lederer B, et al.: Management of breast cancer patients with chemotherapy-induced neutropenia or febrile neutropenia. Breast Care (Basel). 2014 Apr;9(4):239-45.
9. Lee YM, Lockwood C. Prognostic factors for risk stratification of adult cancer patients with chemotherapy-induced febrile neutropenia: a systematic review and meta-analysis. Int J Nurs Pract. 2013 Dec;19(6):557-76.
10. Lyman GH, Abella E, Pettengell R. Risk factors for febrile neutropenia among patients with cancer receiving chemotherapy: A systematic review. Crit Rev Oncol Hematol. 2014 Jun;90(3):190-9.
11. Lyman GH, Dale DC, Culakova E, et al.: The impact of the granulocyte colony-stimulating factor on chemotherapy dose intensity and cancer survival: a systematic review and meta-analysis of randomized controlled trials. Ann Oncol. 2013 Oct;24(10):2475-84.



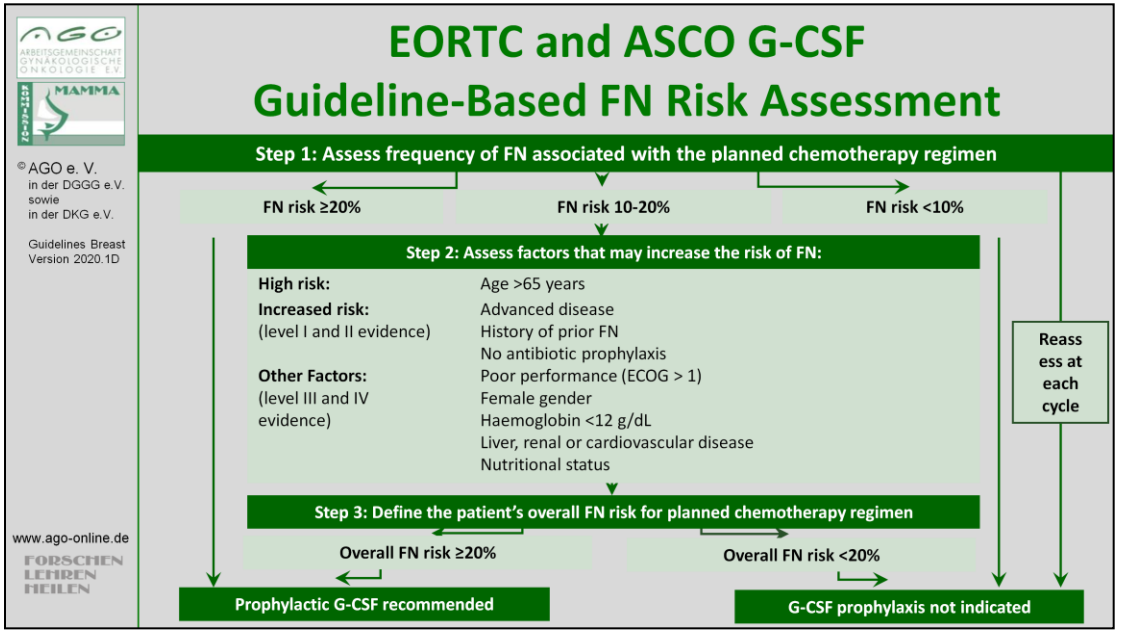
1. Klastersky J, de Naurois J, Rolston K, et al.:Management of febrile neutropaenia: Esmo clinical practice guidelines. Ann Oncol 2016;27:v111-v118.
2. Schmidt-Hieber M, Bierwirth J, Buchheidt D, Cornely OA, Hentrich M, Maschmeyer G, Schalk E, Vehreschild JJ, Vehreschild M, Group AW: Diagnosis and management of gastrointestinal complications in adult cancer patients: 2017 updated evidence-based guidelines of the infectious diseases working party (agiho) of the german society of hematology and medical oncology (dgho). Annals of hematology 2018;97:31-49.
3. Flowers CR, Seidenfeld J, Bow EJ et al.: Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American society of clinical oncology clinical practice guideline. J Clin Oncol. 2013 Feb 20;31(6):794-810.
4. Talcott JA, Yeap BY, Clark JA, et al.: Safety of early discharge for low-risk patients with febrile neutropenia: a multicenter randomized controlled trial. J Clin Oncol. 2011 Oct 20;29(30):3977-83
5. Freifeld AG, Sepkowitz KA. No place like home? Outpatient management of patients with febrile neutropenia and low risk. J Clin Oncol 2011 Oct 20;29(30):3952-4.
6. de Naurois J, Novitzky-Basso I, Gill MJ, et al, . Management of febrile neutropenia: ESMO Clinical Practice Guidelines. Ann Oncol 2010;21(Suppl 5):v252-6

7. Aapro MS, Bohlius J, Cameron DA et al.: 2010 update of EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumours. Eur J Cancer 2011;47(1):8-32.
8. Paul M, Yahav D, Fraser A, et al.: Empirical antibiotic monotherapy for febrile neutropenia: systematic review and meta- analysis of randomized controlled trials. J Antimicrob Chemother 2006;57:176-189
9. Malik IA, Khan WA, Karim M, et al. Feasibility of outpatient management of fever in cancer patients with low-risk neutropenia: results of a prospective randomized trial. Am J Med 1995;98:224-231.



Kochanek M, Schalk E, von Bergwelt-Baildon M, et al : Management of sepsis in neutropenic cancer patients: 2018 guidelines from the infectious diseases working party (agiho) and intensive care working party (ichop) of the german society of hematology and medical oncology (dgho). Annals of hematology 2019;98:1051-1069.

Vossen MG, Milacek C, Thalhammer F: Empirical antimicrobial treatment in haemato-/oncological patients with neutropenic sepsis. ESMO open 2018;3:e000348.

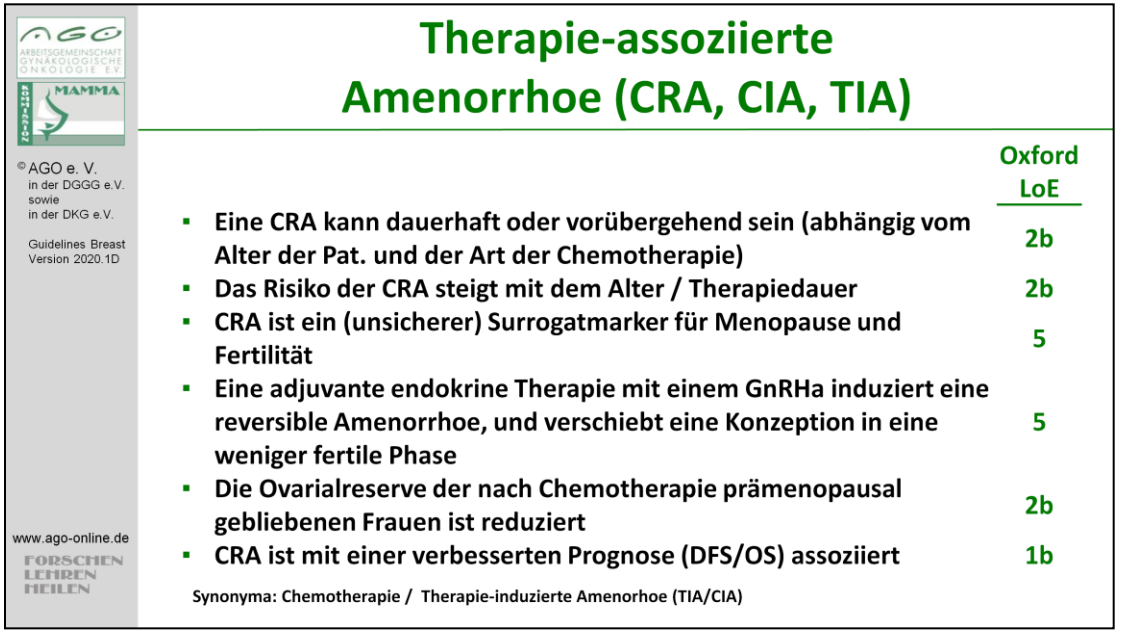


EORTC and ASCO G-CSF Guideline-Based FN Risk Assessment

1. Aapro MS, Bohlius J, Cameron DA, et al.: European Organisation for Research and Treatment of Cancer. 2010 update of EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumours. Eur J Cancer. 2011 Jan;47(1):8-32.
2. Smith TJ, Bohlke K, Lyman GH, et al.: Recommendations for the use of wbc growth factors: American society of clinical oncology clinical practice guideline update. J Clin Oncol 2015;33:3199-3212.
3. Lee YM, Lockwood C. Prognostic factors for risk stratification of adult cancer patients with chemotherapy-induced febrile neutropenia: a systematic review and meta-analysis. Int J Nurs Pract. 2013 Dec;19(6):557-76.
4. Lyman GH, Abella E, Pettengell R. Risk factors for febrile neutropenia among patients with cancer receiving chemotherapy: A systematic review. Crit Rev Oncol Hematol. 2014 Jun;90(3):190-9.
5. Lyman GH. A comparison of international guidelines for the prevention of chemotherapy-induced neutropenia. Curr Opin Hematol. 2011 Jan;18(1):1-10.

Guidelines Breast
Version 2020.1D

4. Endokrine Erkrankungen



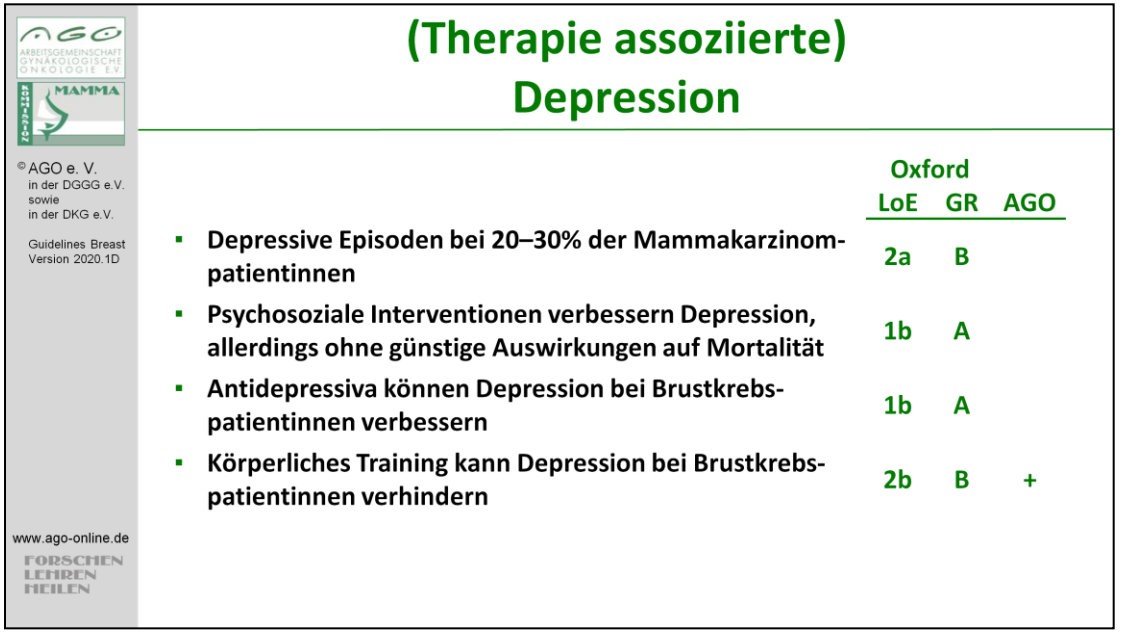
1. Abe A, Kuwahara A, Iwasa T, et al. A survey on fertility management in young women of reproductive age treated with chemotherapy. Int J Clin Oncol. 2016 Dec;21(6):1183-1190.
2. Anderson RA, Mansi J, Coleman RE, et al. The utility of anti-Müllerian hormone in the diagnosis and prediction of loss of ovarian function following chemotherapy for early breast cancer. Eur J Cancer. 2017 Dec;87:58-64.
3. Xue C, Wei W, Sun P, et al.: Pretreatment anti-mullerian hormone-based nomogram predicts menstruation status after chemotherapy for premenopausal women with hormone receptor-positive early breast cancer. Breast Cancer Res Treat 2019;173:619-628.
4. Ruddy KJ, Schaid DJ, Partridge AH, et al.: Genetic predictors of chemotherapy-related amenorrhea in women with breast cancer. Fertility and sterility 2019;112:731-739.e731.
5. Wakimoto Y, Fukui A, Wakimoto G, et al: Association between spontaneous ovulation and serum anti-mullerian hormone levels in a premature ovarian insufficiency patient after a multimodal treatment for breast cancer. The journal of obstetrics and gynaecology research 2019;45:2297-2301.
6. Chung C. Risk of ovarian function recovery should be considered when switching from treatment with adjuvant tamoxifen to aromatase inhibitor therapy in women with chemotherapy-induced amenorrhea. CA Cancer J Clin. 2018 Jan;68(1):5-6.
7. Druz M, Gimenes D, Fanelli M(2010) Fertility preservation in women with breast cancer undergoing adjuvant chemotherapy: a systematic review. Fertil Steril 94: 138-43.

8. Fréour T, Barrière P, Masson D. Anti-müllerian hormone levels and evolution in women of reproductive age with breast cancer treated with chemotherapy. Eur J Cancer. 2017 Mar;74:1-8
9. Ganz PA, Land SR, Geyer CE Jr, et al:. Menstrual history and quality-of-life outcomes in women with node-positive breast cancer treated with adjuvant therapy on the NSABP B-30 trial. J Clin Oncol. 2011 Mar 20;29(9):1110-6.
10. Gerber B, von Minckwitz G, Stehle H et al: Effect of luteinizing hormone-releasing hormone agonist on ovarian function after modern adjuvant breast cancer chemotherapy: the GBG 37 ZORO study. J Clin Oncol 29:2334-2341, 2011
11. Howard-Anderson J, Ganz PA, Bower JE, et al. Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: a systematic review. J Natl Cancer Inst 2012; 104: 386–405.
12. Kim H, Han W, Ku SY, et al.: Feature of amenorrhea in postoperative tamoxifen users with breast cancer. J Gynecol Oncol. 2017 Mar;28(2):e10.
13. Lambertini M, Ceppi M, Poggio F, et al.: Ovarian suppression using luteinizing hormone-releasing hormone agonists during chemotherapy to preserve ovarian function and fertility of breast cancer patients: a meta-analysis of randomized studies. Ann Oncol. 2015 Dec;26(12):2408-19. doi: 10.1093/annonc/mdv374. Epub 2015 Sep 7.
14. Letourneau JM, Ebbel EE, Katz PP et al.: Acute ovarian failure underestimates agespecific reproductive impairment for young women undergoing chemotherapy for cancer. Cancer 2012; 118: 1933–1939.
15. Liem GS, Mo FK, Pang E, et al.: Chemotherapy-Related Amenorrhea and Menopause in Young Chinese Breast Cancer Patients: Analysis on Incidence, Risk Factors and Serum Hormone Profiles. PLoS One. 2015 Oct 20;10(10):e0140842. doi: 10.1371/journal.pone.0140842. eCollection 2015.
16. Swain S, Jeong J, Geyer CJ et al.(2010) Longer therapy, iatrogenic amenorrhoe, and survival in early breast cancer. N Engl J Med 362: 2053-65.
17. Swain S, Jeong J, Wolmark N (2010) Amenorrhoe from the breast cancer therapy - not a matter of dose. New Engl J Med 353: 2268-70
18. Tiong V, Rozita AM, Taib NA et al. Incidence of chemotherapy-induced ovarian failure in premenopausal women undergoing chemotherapy for breast cancer. World J Surg 2014; 38: 2288–2296
19. van Hellemond IEG, Vriens IJH, Peer PGM, et al.: Ovarian Function Recovery During Anastrozole in Breast Cancer Patients With Chemotherapy-Induced Ovarian Function Failure. JNCI J Natl Cancer Inst (2017) 109(12): djx074
20. Vriens IJ, De Bie AJ, Aarts MJ, et al. The correlation of age with chemotherapy-induced ovarian function failure in breast cancer patients. Oncotarget. 2017 Feb 14;8(7):11372-11379.

Nebenwirkungen nach Organsystemen
Inzidenz, Prävention, Therapie

5. Psychiatrische Erkrankungen

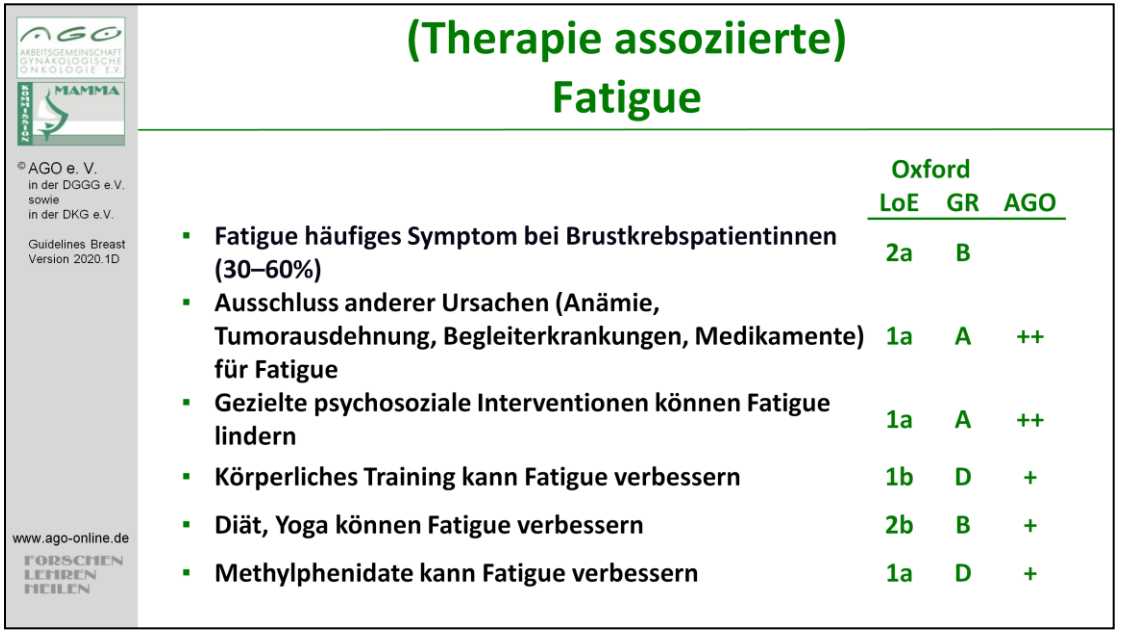
- Depression
- Fatigue
- Kognitive Störungen
- Schlafstörungen



Statements 1-4

1. Desautels C, Savard J, Ivers H, et al.: Treatment of depressive symptoms in patients with breast cancer: A randomized controlled trial comparing cognitive therapy and bright light therapy. Health Psychol. 2018 Jan;37(1):1-13.
2. Huang Z, Zhao J, Ding K, Lv Y, Zhang C, Chao HH, Li CS, Cheng H: Depression involved in self-reported prospective memory problems in survivors of breast cancer who have received chemotherapy. Medicine (Baltimore) 2019;98:e15301.
3. Calderon C, Carmona-Bayonas A, Hernandez R, et al. Effects of pessimism, depression, fatigue, and pain on functional health-related quality of life in patients with resected non-advanced breast cancer. Breast 2019;44:108-12.
4. Jacob L, Kalder M, Kostev K. Incidence of depression and anxiety among women newly diagnosed with breast or genital organ cancer in Germany. Psychooncology. 2017 Oct;26(10):1535-1540.
5. Jafari A, Goudarzian AH, Bagheri Nesami M. Depression in Women with Breast Cancer: A Systematic Review of Cross-Sectional Studies in Iran. Asian Pac J Cancer Prev. 2018 Jan 27;19(1):1-7.
6. Kostev K, Jacob L, Kalder M. Risk of depression, anxiety, and adjustment disorders in women with a suspected but unconfirmed diagnosis of breast or genital organ cancer in Germany. Cancer Causes Control. 2017 Oct;28(10):1021-1026
7. Patsou ED, Alexias GD, Anagnostopoulos FG, et al.: Effects of physical activity on depressive symptoms during breast cancer survivorship: a meta-analysis of randomised control trials. ESMO Open. 2017 Dec 11;2(5):e000271.
8. Brown JC, Huedo-Medina TB, Pescatello LS, et al: The efficacy of exercise in reducing depressive symptoms among cancer

survivors: a meta-analysis. PLoS One. 2012;7(1):e30955. doi: 10.1371/journal.pone.0030955.
9. Hart SL, Hoyt MA, Diefenbach M, et al.: Meta-analysis of efficacy of interventions for elevated depressive symptoms in adults diagnosed with cancer. J Natl Cancer Inst. 2012 Jul 3;104(13):990-1004. doi: 10.1093/jnci/djs256.
10. Iovieno N, Tedeschini E, Ameral VE, et al: Antidepressants for major depressive disorder in patients with a co-morbid axis-III disorder: a meta-analysis of patient characteristics and placebo response rates in randomized controlled trials. Int Clin Psychopharmacol. 2011 Mar;26(2):69-74. doi: 10.1097/YIC.0b013e328340775e.
11. Eyding D, Lelgemann M, Grouven U, et al: Reboxetine for acute treatment of major depression: systematic review and meta-analysis of published and unpublished placebo and selective serotonin reuptake inhibitor controlled trials. BMJ. 2010 Oct 12;341:c4737. doi: 10.1136/bmj.c4737.
12. Chen X, Lu W, Zheng Y, et al: Exercise, Tea Consumption, and Depression Among Breast Cancer Survivors. J Clin Oncol 28: 991-998, 2010
13. Bower JE: Behavioral symptoms in patients with breast cancer and survivors. J Clin Oncol. 26:768-777, 2008
14. Gallo JJ, Bogner HR, Morales KH, et al: The effect of a primary care practice-based depression intervention on mortality in older adults: A randomized trial. Ann Intern Med 146:689-698, 2007
15. Bardwell WA, Natarajan L, Dimsdale JE, et al: Objective cancer-related variables are not associated with depressive symptoms in women treated for early-stage breast cancer. J Clin Oncol 24:2420-2427, 2006
16. Blaney JM,Lowe-Strong A, Rankin-Watt J, et al.(2013). Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: a questionnaire-survey. Psychooncology, 22, 186-94.
17. Tabrizi FM, Radfar M, Taei Z (2016). Effects of supportive-expressive discussion groups on loneliness, hope and quality of life in breast cancer survivors: a randomized control trial. Psychooncology, 25, 1057-63.



Fatigue is frequently present…

1. Bower JE, Ganz PA, Irwin MR, et al.: Fatigue and gene expression in human leukocytes: increased NF-κB and decreased glucocorticoid signaling in breast cancer survivors with persistent fatigue. Brain Behav Immun. 2011 Jan;25(1):147-50.
2. Blaney JM, Lowe-Strong A, Rankin-Watt J, et al.: Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: a questionnaire-survey. Psychooncology. 2013 Jan;22(1):186-94. doi: 10.1002/pon.2072. Epub 2011 Oct 6.
3. Minton ,Stone: How common is fatigue in disease-free breast cancer survivors? A systematic review of the literature. Breast Cancer Res Treat 112: 5-13, 2008
4. Bower JE: Behavioral symptoms in patients with breast cancer and survivors. J Clin Oncol. 26:768-777, 2008
5. Bower JE, Ganz PA, Desmond KA, et al: Fatigue in long-term breast carcinoma survivors: A longitudinal investigation. Cancer 106:751-758, 2006
6. Lawrence DP, Kupelnick B, Miller K, et al: Evidence report on the occurrence, assessment, and treatment of fatigue in cancer patients. J Natl Cancer Inst Monogr 32:40-50, 2004
7. NCCN Guidlinesin Oncology. Survivorship. Version 1.2016. NCCN.org
8. Peoples AR, Roscoe JA, Block RC, et al.: Nausea and disturbed sleep as predictors of cancer-related fatigue in breast cancer patients: a multicenter NCORP study. Support Care Cancer. 2016 Dec 20. [Epub ahead of print]

9. Zick SM,Colacino J, Cornellier M, et al.: Fatigue reduction diet in breast cancer survivors: a pilot randomized clinical trial. Breast Cancer Res Treat. 2017 Jan;161(2):299-310. doi: 10.1007/s10549-016-4070-y. Epub 2016 Dec 2.
10. Sadeghi E, Gozali N, Moghaddam Tabrizi F. Effects of Energy Conservation Strategies on Cancer Related Fatigue and Health Promotion Lifestyle in Breast Cancer Survivors: a Randomized Control Trial. Asian Pac J Cancer Prev. 2016 Oct 1;17(10):4783-4790
11. Wang XS, Woodruff JF (2015). Cancer-related and treatment-related fatigue. Gynecol Oncol, 136, 446-52.
12. Husson O, Mols F, Van de Poll-Franse L, et al (2015). Variation in fatigue among 6011 (long-term) cancer survivors and a normative population: a study from the population-based PROFILES registry. Support Care Cancer, 23, 2165-74.
13. Jones SM, Ludman EJ, Mc-Corkle R, et al. (2015). A differential item function analysis of somatic symptoms of depression in people with cancer. J Affect Disord, 170, 131-37.
14. Tabrizi FM, Radfar M (2015). Fatigue, sleep quality, and disability in relation to quality of life in multiple sclerosis. Int J MS Care, 17, 268-74.

Psycho-social interventions…

1. Goedendorp MM, Gielissen MFM, Verhagen CAHHVM, et al.: Psychosocial interventions for reducing fatigue during cancer treatment in adults. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD006953. DOI: 10.1002/14651858.CD006953.pub2
2. Stanton AL, Ganz PA, Kwan L, et al: Outcomes from the Moving Beyond Cancer psychoeducational, randomized, controlled trial with breast cancer patients. J Clin Oncol 23:6009-6018, 2005
3. Reif KU, de Vries U, Petermann F, et al.(2013). A patient education program is effective in reducing cancer-related fatigue: a multi-centre randomised two-group waiting-list controlled intervention trial. Eur J Oncol Nurs, 17, 204-13.
4. Blaney JM,Lowe-Strong A, Rankin-Watt J, et al.(2013). Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: a questionnaire-survey. Psychooncology, 22, 186-94.
5. Donovan KA, Stein KD, Lee M, et al (2015). Systematic review of the multidimensional fatigue symptom inventory-short form.Support Care Cancer, 23, 191-212.
6. Peters ME, Goedendorp MM, Verhagen SA, et al.(2014). Exploring the contribution of psychosocial factors to fatigue in patients with advanced incurable cancer. Psychooncology, 23, 773-9.
7. Tabrizi FM, Radfar M, Taei Z (2016). Effects of supportive-expressive discussion groups on loneliness, hope and quality of life in breast cancer survivors: a randomized control trial. Psychooncology, 25, 1057-63.

Physical exercise…..

1. Furmaniak AC, Menig M, Markes MH.: Exercise for women receiving adjuvant therapy for breast cancer. Cochrane Database Syst Rev. 2016.
2. Park SS, Park HS, Jeong H, Kwak HB, No MH, Heo JW, et al. Treadmill Exercise Ameliorates Chemotherapy-Induced Muscle Weakness and Central Fatigue by Enhancing Mitochondrial Function and Inhibiting Apoptosis. International neurourology journal 2019;23(Suppl 1):S32-39.
3. Mijwel S, Jervaeus A, Bolam KA, Norrbom J, Bergh J, Rundqvist H, et al. High-intensity exercise during chemotherapy induces beneficial effects 12 months into breast cancer survivorship. Journal of cancer survivorship : research and practice 2019.
4. Winters-Stone KM, Moe EL, Perry CK, et al.: Enhancing an oncologist's recommendation to exercise to manage fatigue levels in breast cancer patients: a randomized controlled trial. Support Care Cancer. 2018 Mar;26(3):905-912.
5. Cramer H, Lauche R, Klose P, et al.: Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. Cochrane Database Syst Rev. 2017 Jan 3;1:CD010802.
6. Cramp F, Byron-Daniel J.: Exercise for the management of cancer-related fatigue in adults. Cochrane Database Syst Rev. 2012 Nov 14;11:CD006145. doi: 10.1002/14651858.CD006145.pub3.
7. Mishra SI, Scherer RW, Snyder C, et al.: Exercise interventions on health-related quality of life for people with cancer during active treatment. Cochrane Database Syst Rev. 2012 Aug 15;8:CD008465. doi: 10.1002/14651858.CD008465.pub2.
8. Mishra SI, Scherer RW, Geigle PM, et al.: Exercise interventions on health-related quality of life for cancer survivors. Cochrane Database Syst Rev. 2012 Aug 15;8:CD007566. doi: 10.1002/14651858.CD007566.pub2. Review.
9. Buffart LM, van Uffelen JG, Riphagen II, et al.: Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials.BMC Cancer. 2012 Nov 27;12(1):559. [Epub ahead of print]
10. Fong DY, Ho JW, Hui BP, Lee AM, et al.: Physical activity for cancer survivors: meta-analysis of randomised controlled trials. BMJ. 2012 Jan 30;344:e70. doi: 10.1136/bmj.e70.
11. Goedendorp MM, Peters ME, Gielissen MFM, et al: Is increasing physical activity necessary to diminish fatigue during cancer treatment? Comparing cognitive behavior therapy and a brief nursing intervention with usual care in a multicenter randomized controlled trial. Oncologist 15:1122-1132, 2010
12. Markes M, Brockow T, Resch K-L. Exercise for women receiving adjuvant therapy for breast cancer. Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD005001. DOI: 10.1002/14651858.CD005001.pub2
13. Bower JE, Garte D, Sternlieb B et al. Yoga for persistent fatigue in breast cancer survivors: A randomized controlled trial. Cancer 2011 Dec 16. Doi: 10.1002/cncr26702. (Epub ahead of print)

14. Irwin ML, Cartmel B, Harrigan M, et al.: Effect of the LIVESTRONG at the YMCA exercise program on physical activity, fitness, quality of life, and fatigue in cancer survivors. Cancer. 2016 Nov 28. doi: 10.1002/cncr.30456. [Epub ahead of print]
15. Cramer H, Lauche R, Klose P, et al.: Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. Cochrane Database Syst Rev. 2017 Jan 3;1:CD010802. doi: 10.1002/14651858.CD010802.pub2. [Epub ahead of print]
16. Irwin ML, Cartmel B, Harrigan M, et al. Effect of the LIVESTRONG at the YMCA exercise program on physical activity, fitness, quality of life, and fatigue in cancer survivors. Cancer. 2016 Nov 28. doi: 10.1002/cncr.30456.
17. Rogers LQ, Courneya KS, Anton PM, et al. Effects of a multicomponent physical activity behavior change intervention on fatigue, anxiety, and depressive symptomatology in breast cancer survivors: randomized trial. Psychooncology. 2016 Aug 17. doi: 10.1002/pon.4254. [Epub ahead of print]
18. Phillips SM, Lloyd GR, Awick EA, et al.: Relationship between self-reported and objectively measured physical activity and subjective memory impairment in breast cancer survivors: role of self-efficacy, fatigue and distress. Psychooncology. 2016 Jul 8. doi: 10.1002/pon.4156. [Epub ahead of print]
19. Galiano-Castillo N, Cantarero-Villanueva I, Fernández-Lao C, et al.: Telehealth system: A randomized controlled trial evaluating the impact of an internet-based exercise intervention on quality of life, pain, muscle strength, and fatigue in breast cancer survivors. Cancer. 2016 Oct 15;122(20):3166-3174. doi: 10.1002/cncr.30172. Epub 2016 Jun 22.
20. Zhu G, Zhang X, Wang Y, et al.: Effects of exercise intervention in breast cancer survivors: a meta-analysis of 33 randomized controlled trails. Onco Targets Ther. 2016 Apr 13;9:2153-68. doi: 10.2147/OTT.S97864. eCollection 2016.

Methylphenidate…

1. Bruera E, Valero V, Driver L, et al: Patient-controlled methylphenidate for cancer fatigue: A double-blind, randomized, placebo-controlled trial. J Clin Oncol 24:2073-2078, 2006
2. Peuckmann-Post V, Elsner F, Krumm N et al: Pharmacological treatments for fatigue associated with palliative care. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD006788. DOI: 10.1002/14651858.CD006788.pub2
3. Vance DE, Frank JS, Bail J, et al.: Interventions for Cognitive Deficits in Breast Cancer Survivors Treated With Chemotherapy. Cancer Nurs. 2017 Jan/Feb;40(1):E11-E27.

Therapiebedingte kognitive Störungen (sog. „Chemobrain“) häufig beschrieben

1. Jim HS, Phillips KM, Chait S, 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. doi: 10.1200/JCO.2011.39.5640.
2. Deprez S, Amant F, Smeets A et al: Longitudinal assessment of chemotherapy induced structural chan ges in cerebral white matter and its correlation with impaired cognitive function. J Clin Oncol 2011 Dec 19. (Epub ahead of print)
3. Debess J, Riis JØ, Engebjerg MC, et al.: Cognitive function after adjuvant treatment for early breast cancer: a population-based longitudinal study. Breast Cancer Res Treat 121:91-100, 2010
4. Schilder CM, Seynaeve C, Beex LV, et al: Effects of tamoxifen and exemestane on cognitive functioning of postmenopausal patients with breast cancer: results from the neuropsychological side study of the tamoxifen and exemestane adjuvant multinational trial. J Clin Oncol 28:1294-300, 2010
5. Bower JE: Behavioral symptoms in patients with breast cancer and survivors. J Clin Oncol. 26:768-777, 2008
6. Vardy J, Rourke S, Tannock IF: Evaluation of cognitive function associated with chemotherapy: A review of published studies and recommendations for future research. J Clin Oncol 25:2455-2463, 2007
7. Silverman DH, Dy CJ, Castellon SA, et al: Altered frontocortical, cerebellar, and basal ganglia activity in adjuvant-treated breast cancer survivors 5-10 years after chemotherapy. Breast Cancer Res Treat 103:303-311, 2007
8. Ahles TA, Saykin AJ: Candidate mechanisms for chemotherapy-induced cognitive changes. Nat Rev Cancer 7:192-201, 2007

9. Stewart A, Bielajew C, Collins B, et al: A meta-analysis of the neuropsychological effects of adjuvant chemotherapy treatment in women treated for breast cancer. Clin Neuropsychol 20:76-89, 2006
10. Fan HG, Houede-Tchen N, Yi QL, et al: Fatigue, menopausal symptoms, and cognitive function in women after adjuvant chemotherapy for breast cancer: 1- and 2-year follow-up of a prospective controlled study. J Clin Oncol 23:8025-8032, 2005
11. Paquet L, Verma S, Collins B, et al.: Testing a novel account of the dissociation between self-reportedmemory problems and memory performance in chemotherapy treated breast cancer survivors. Psychooncology. 2017 Jan 27. doi: 10.1002/pon.4389. [Epub ahead of print]
12. Orchard TS, Gaudier-Diaz MM, Weinhold KR, et al.: Clearing the fog: a review of the effects of dietary omega-3 fatty acids and added sugars on chemotherapy-induced cognitive deficits. Breast Cancer Res Treat. 2017 Feb;161(3):391-398. doi: 10.1007/s10549-016-4073-8. Epub 2016 Dec 8.
13. Selamat MH, Loh SY, Mackenzie L, et al.: Chemobrain experienced by breast cancer survivors: a meta-ethnography study investigating research and care implications. PLoS One. 2014 Sep 26;9(9):e108002. doi: 10.1371/journal.pone.0108002. eCollection 2014.

<u>Verhaltenstherapie kann kognitive Funktion verbessern</u>

1. Groarke A, Curtis R, Kerin M.: Cognitive-behavioural stress management enhances adjustment in women with breast cancer. Br J Health Psychol. 2012 Dec 4. doi: 10.1111/bjhp.12009. [Epub ahead of print]
2. Cramer H, Lauche R, Paul A, et al.: Mindfulness-based stress reduction for breast cancer-a systematic review and meta-analysis. Curr Oncol. 2012 Oct;19(5):e343-52. doi: 10.3747/co.19.1016.
3. Ferguson RJ, Ahles TA, Saykin AJ, et al: Cognitive-behavioral management of chemotherapy-related cognitive change. Psychooncology 16:772-777, 2007
4. Blaney JM,Lowe-Strong A, Rankin-Watt J, Campbell A, Gracey JH (2013). Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: a questionnaire-survey. Psychooncology, 22, 186-94.
5. Tabrizi FM, Radfar M, Taei Z (2016). Effects of supportive-expressive discussion groups on loneliness, hope and quality of life in breast cancer survivors: a randomized control trial. Psychooncology, 25, 1057-63.
6. Selamat MH, Loh SY, Mackenzie L, et al.: Chemobrain experienced by breast cancer survivors: a meta-ethnography study investigating research and care implications. PLoS One. 2014 Sep 26;9(9):e108002. doi: 10.1371/journal.pone.0108002. eCollection 2014.

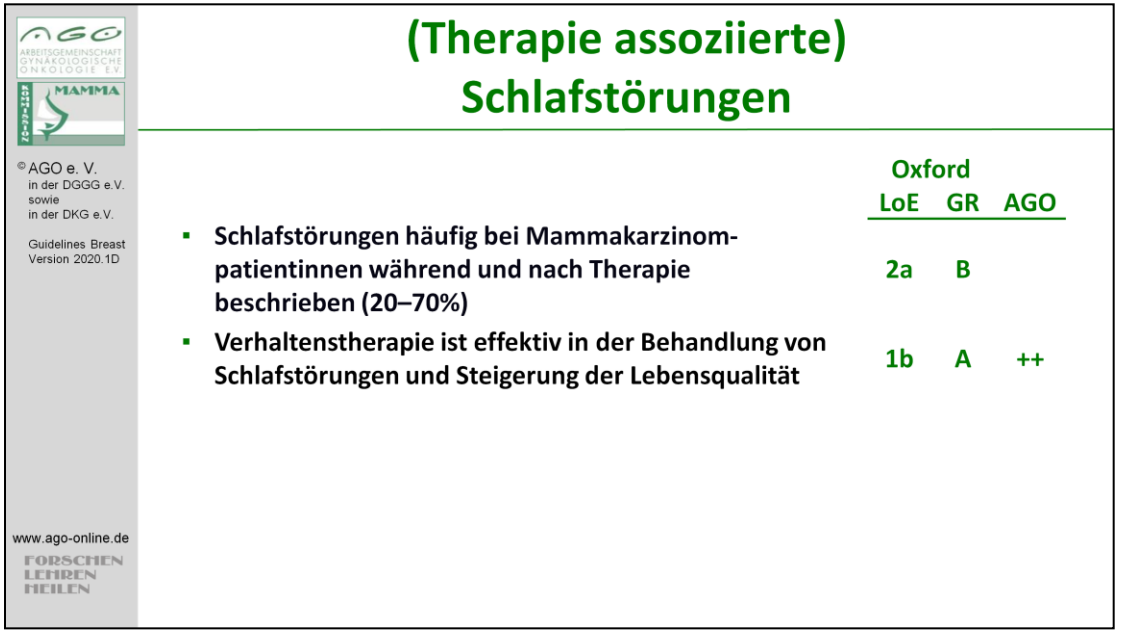
Methylphenidate kann kognitive Funktion bei Patientinnen mit Krebs verbessern

1. Nelson CJ, Nandy N, Roth AJ.: Chemotherapy and cognitive deficits: mechanisms, findings, and potential interventions. Palliat Support Care. 2007 Sep;5(3):273-80.
2. Rozans M, Dreisbach A, Lertora JJ, et al: Palliative uses of methylphenidate in patients with cancer: A review. J Clin Oncol 20:335-339, 2002
3. Vance DE, Frank JS, Bail J, et al.: Interventions for Cognitive Deficits in Breast Cancer Survivors Treated With Chemotherapy. Cancer Nurs. 2017 Jan/Feb;40(1):E11-E27.

Unter Aromatasehemmertherapie wurden kogmitive Störungen beobachtet

1. Underwood EA, Rochon PA, Moineddin R, et al.: Cognitive sequelae of endocrine therapy in women treated for breast cancer: a meta-analysis. Breast Cancer Res Treat. 2017 Dec 20.
2. Zameer S, Vohora D. Effect of aromatase inhibitors on learning and memory and modulation of hippocampal dickkopf-1 and sclerostin in female mice. Pharmacol Rep. 2017 Dec;69(6):1300-1307.
3. Gallicchio L, Calhoun C, Helzlsouer K. A prospective study of aromatase inhibitor therapy initiation and self-reported side effects. Support Care Cancer. 2017 Sep;25(9):2697-2705.
4. Koleck TA, Bender CM, Sereika SM, et al.: Associations between pathologic tumor features and preadjuvant therapy cognitive performance in women diagnosed with breast cancer. Cancer Med. 2017 Feb;6(2):339-348.
5. Zdenkowski N, Tesson S, Lombard J, et al.: Supportive care of women with breast cancer: key concerns and practical solutions. Med J Aust. 2016 Nov 21;205(10):471-475. Review.
6. Li C, Zhou C, Li R. Can Exercise Ameliorate Aromatase Inhibitor-Induced Cognitive Decline in Breast Cancer Patients? Mol Neurobiol. 2016 Aug;53(6):4238-4246.
7. Nugent BD, Sereika SM, Rosenzweig M, et al.: The association between pre-treatment occupational skill level and mood and symptom burden in early-stage, postmenopausal breast cancer survivors during the first year of anastrozole therapy. Support Care Cancer. 2016 Aug;24(8):3401-9.
8. Bright EE, Petrie KJ, Partridge AH, et al.: Barriers to and facilitative processes of endocrine therapy adherence among women with breast cancer. Breast Cancer Res Treat. 2016 Jul;158(2):243-51.
9. Ganz PA, Petersen L, Bower JE, et al.: Impact of Adjuvant Endocrine Therapy on Quality of Life and Symptoms: Observational Data Over 12 Months From the Mind-Body Study. J Clin Oncol. 2016 Mar 10;34(8):816-24.

10. Ganz PA, Cecchini RS, Julian TB, et al.: Patient-reported outcomes with anastrozole versus tamoxifen for postmenopausal patients with ductal carcinoma in situ treated with lumpectomy plus radiotherapy (NSABP B-35): a randomised, double-blind, phase 3 clinical trial. Lancet. 2016 Feb 27;387(10021):857-65.
11. Bakoyiannis I, Tsigka EA, Perrea D, et al.: The Impact of Endocrine Therapy on Cognitive Functions of Breast Cancer Patients: A Systematic Review. Clin Drug Investig. 2016 Feb;36(2):109-18.
12. Frank JS, Vance DE, Triebel KL, et al.: Cognitive Deficits in Breast Cancer Survivors After Chemotherapy and Hormonal Therapy. J Neurosci Nurs. 2015 Dec;47(6):302-12.
13. Le Rhun E, Delbeuck X, Lefeuvre-Plesse C, et al.: A phase III randomized multicenter trial evaluating cognition in post-menopausal breast cancer patients receiving adjuvant hormonotherapy. Breast Cancer Res Treat. 2015 Aug;152(3):569-80.
14. Bender CM, Merriman JD, Gentry AL, Ahrendt GM, Berga SL, Brufsky AM, Casillo FE, Dailey MM, Erickson KI, Kratofil FM, McAuliffe PF, Rosenzweig MQ, Ryan CM, Sereika SM. Patterns of change in cognitive function with anastrozole therapy. Cancer. 2015 Aug 1;121(15):2627-36.
15. Lintermans A, Neven P. Safety of aromatase inhibitor therapy in breast cancer. Expert Opin Drug Saf. 2015 Aug;14(8):1201-11.
16. Berndt U, Leplow B, Schoenfeld R, et al.: Memory and Spatial Cognition in Breast Cancer Patients Undergoing Adjuvant Endocrine Therapy. Breast Care (Basel). 2016 Aug;11(4):240-246.



Sleep disturbances are a common problem….

1. Fontes F, Pereira S, Costa AR, et al.: The impact of breast cancer treatments on sleep quality 1 year after cancer diagnosis. Support Care Cancer. 2017 Nov;25(11):3529-3536.
2. Cramer H, Lauche R, Klose P, et al.: Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. Cochrane Database Syst Rev. 2017 Jan 3;1:CD010802.
3. Schmidt ME, Wiskemann J, Schneeweiss A, et al.: Determinants of physical, affective, and cognitive fatigue during breast cancer therapy and 12 months follow-up. Int J Cancer. 2018 Mar 15;142(6):1148-1157.
4. Dhruva A, Paul SM, Cooper BA, et al.: A longitudinal study of measures of objective and subjective sleep disturbance in patients with breast cancer before, during, and after radiation therapy. J Pain Symptom Manage. 2012 Aug;44(2):215-28.
5. Liu L, Mills PJ, Rissling M, et al.: Fatigue and sleep quality are associated with changes in inflammatory markers in breast cancer patients undergoing chemotherapy. Brain Behav Immun. 2012 Jul;26(5):706-13
6. McChargue DE, Sankaranarayanan J, Visovsky CG, et al.: Predictors of adherence to a behavioral therapy sleep intervention during breast cancer chemotherapy. Support Care Cancer. 2012 Feb;20(2):245-52.
7. Bower JE, Ganz PA, Irwin MR et al: Inflammation and behavioural symptoms after breast cancer treatment: do fatigue, depression, and sleep disturbances share a common underlying mechanism? J Clin Oncol 29:3517-3522,2011
8. Palesh OG, Roscoe JA, Mustian KM, et al: Prevalence, demographics, and psychological associations of sleep disruption in

patients with cancer: University of Rochester Cancer Center-Community Clinical Oncology Program. J Clin Oncol 28:292-298, 2010
9. Bower JE: Behavioral symptoms in patients with breast cancer and survivors. J Clin Oncol. 26:768-777, 2008
10. Ancoli-Israel S, Liu L, Marler MR, et al: Fatigue, sleep, and circadian rhythms prior to chemotherapy for breast cancer. Support Care Cancer 14:201-209, 2006
11. Blaney JM,Lowe-Strong A, Rankin-Watt J, et al.(2013). Cancer survivors' exercise barriers, facilitators and preferences in the context of fatigue, quality of life and physical activity participation: a questionnaire-survey. Psychooncology, 22, 186-94.
12. Tabrizi FM, Radfar M, Taei Z (2016). Effects of supportive-expressive discussion groups on loneliness, hope and quality of life in breast cancer survivors: a randomized control trial. Psychooncology, 25, 1057-63.

Behavioral therapies have demonstrated efficacy…..

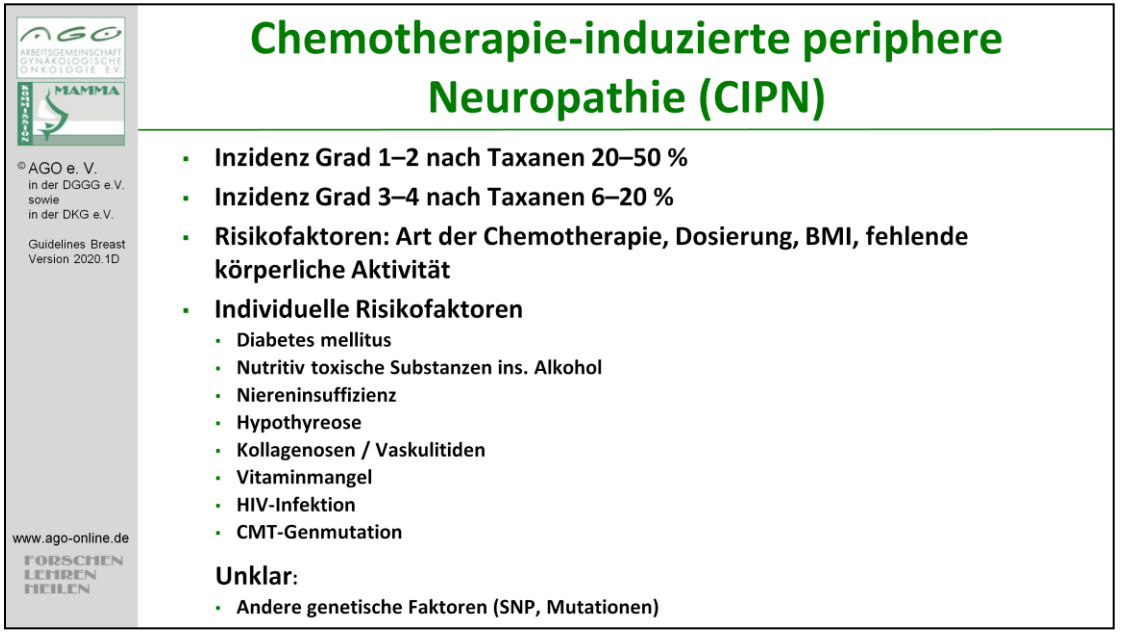
1. Berger AM, Kuhn BR, Farr LA, et al: One-year outcomes of a behavioral therapy intervention trial on sleep quality and cancer-related fatigue. J Clin Oncol 27: 6033-6040, 2009
2. Savard J, Simard S, Ivers H, et al: Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: Sleep and psychological effects. J Clin Oncol 23:6083-6096, 2005
3. Smith MT, Perlis ML, Park A, et al: Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia. Am J Psychiatry 159:5-11, 2002

Guidelines Breast
Version 2020.1D

Nebenwirkungen nach Organsystemen
Inzidenz, Prävention, Therapie

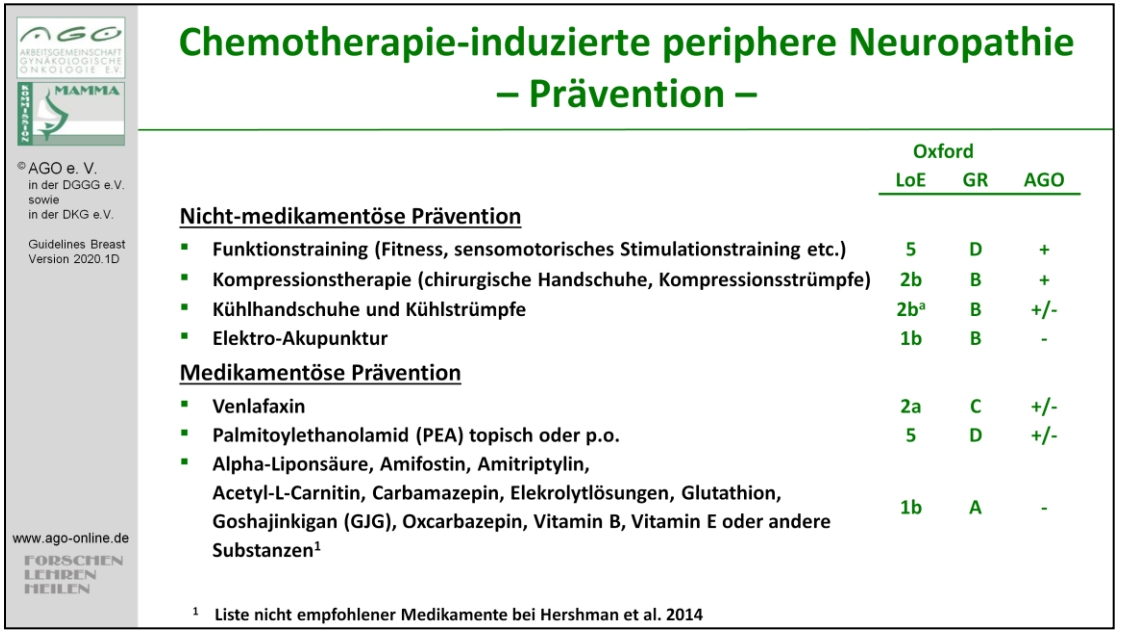
6. Erkrankungen des Nervensystems

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



1. Hershman DL, Lacchetti C, Dworkin RH, et al.: American Society of Clinical Oncology. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014 Jun 20;32(18):1941-67.
2. Hu LY, Mi WL, Wu GC, et al.: Prevention and Treatment for Chemotherapy-Induced Peripheral Neuropathy: Therapies Based on CIPN Mechanisms. Current Neuropharmacology, 2018, 16, 1-12
3. Gewandter JS, Kleckner AS, Marshall JH, Brown JS, Curtis LH, Bautista J, Dworkin RH, Kleckner IR, Kolb N, Mohile SG, Mustian KM: Chemotherapy-induced peripheral neuropathy (cipn) and its treatment: An nih collaboratory study of claims data. Support Care Cancer 2019.
4. Majithia N, Temkin SM, Ruddy KJ, et al.: National Cancer Institute-supported chemotherapy-induced peripheral neuropathy trials: outcomes and lessons. Support Care Cancer. 2016 Mar;24(3):1439-47. doi: 10.1007/s00520-015-3063-4. Epub 2015 Dec 19.
5. Greenlee H, Hershman DL, Shi Z, et al.: BMI, Lifestyle Factors and Taxane-Induced Neuropathy in Breast Cancer Patients: The Pathways Study. J Natl Cancer Inst. 2016 Oct 28;109(2). pii: djw206. Print 2017 Feb.
6. Smith, E. M., H. Pang, C. Cirrincione, S., et al. (2013). "Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced painful peripheral neuropathy: a randomized clinical trial." JAMA 309(13): 1359-1367.
7. Cliff J, Jorgensen AL, Lord R, et al.: The molecular genetics of chemotherapy-induced peripheral neuropathy: A systematic review and meta-analysis. Crit Rev Oncol Hematol. 2017 Dec;120:127-140.

8. S3 Leitlinie Supportive Therapie: Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.1, 2017, AWMF Registernummer: 032/054OL, http://leitlinienprogramm-onkologie.de/Supportive-Therapie.95.0.html (Zugriff 29. Januar 2018)



Reviews/Leitlinien

1. Hershman DL, Lacchetti C, Dworkin RH, et al.: American Society of Clinical Oncology. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014 Jun 20;32(18):1941-67.
2. Ibrahim EY, Ehrlich BE: Prevention of chemotherapy-induced peripheral neuropathy: A review of recent findings. Crit Rev Oncol Hematol 2019;145:102831.
3. Hu LY, Mi WL, Wu GC, et al.: Prevention and Treatment for Chemotherapy-Induced Peripheral Neuropathy: Therapies Based on CIPN Mechanisms. Current Neuropharmacology, 2018, 16, 1-12
4. Majithia N, Temkin SM, Ruddy KJ, et al.: National Cancer Institute-supported chemotherapy-induced peripheral neuropathy trials: outcomes and lessons. Support Care Cancer. 2016 Mar;24(3):1439-47. doi: 10.1007/s00520-015-3063-4. Epub 2015 Dec 19.
5. Greenlee H, Hershman DL, Shi Z, et al.: BMI, Lifestyle Factors and Taxane-Induced Neuropathy in Breast Cancer Patients: The Pathways Study. J Natl Cancer Inst. 2016 Oct 28;109(2). pii: djw206. Print 2017 Feb.
6. Pachman DR, Barton DL, Watson JC, et al.: Chemotherapy-induced peripheral neuropathy: prevention and treatment. Clin Pharmacol Ther. 2011 Sep;90(3):377-87.
7. Schuler U, Heller S. Chemotherapy-induced peripheral neuropathy and neuropathic pain. Schmerz. 2017 Aug;31(4):413-425.

8. Smith, E. M., H. Pang, C. Cirrincione, et al.(2013). "Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced painful peripheral neuropathy: a randomized clinical trial." JAMA 309(13): 1359-1367.
9. Cliff J, Jorgensen AL, Lord R, et al. The molecular genetics of chemotherapy-induced peripheral neuropathy: A systematic review and meta-analysis. Crit Rev Oncol Hematol. 2017 Dec;120:127-140.
10. D'Alessandro EG, Nebuloni Nagy DR, de Brito CMM, et al: Acupuncture for chemotherapy-induced peripheral neuropathy: A randomised controlled pilot study. BMJ Support Palliat Care 2019.

Nicht-medikamentöse Prävention

Funktionstraining

1. Kleckner I, Kamen JS, Peppone LJ et al (2016) A URCC NCORP nationwide randomized controlled trial investigating the effect of exercise on chemotherapy-induced peripheral neuropathy in 314 cancer patients. JClinOncol34(suppl): abstr 10000). http://meetinglibrary. asco.org/content/170470-176.
2. Kleckner IR, Kamen C, Gewandter JS, et al.: Effects of exercise during chemotherapy on chemotherapy-induced peripheral neuropathy: a multicenter, randomized controlled trial. Support Care Cancer. 2017 Dec 14.
3. Streckmann F, Balke M, Lehmann HC, et al.: The preventive effect of sensorimotor- and vibration exercises on the onset of Oxaliplatin- or vinca-alkaloid induced peripheral neuropathies - STOP. BMC Cancer. 2018 Jan 10;18(1):62.

Kompression

1. Tsuyuki S, Senda N, Kanng Y, et al.: Evaluation of the effect of compression therapy using surgical gloves on nanoparticle albumin-bound paclitaxel-induced peripheral neuropathy: a phase II multicenter study by the Kamigata Breast Cancer Study Group. Breast Cancer Res Treat. 2016 Nov;160(1):61-67.
2. Ohno T, Mine T, Yoshioka H, et al.: Management of peripheral neuropathy induced by nab-paclitaxel treatment for breast cancer. Anticancer Res. 2014 Aug;34(8):4213-6.

Kühlung

1. Hanai A, Ishiguro H, Sozu T et al. (2016) The effects of frozen gloves and socks on paclitaxel-induced peripheral neuropathy among patientswith breast cancer: A selfcontrolled clinical trial. J ClinOncol 34(suppl): (abstr 10022).

http://meetinglibrary.asco.org/content/166655-176.
2. Sundar R, Bandla A, Tan SS, et al.: Limb Hypothermia for Preventing Paclitaxel-Induced Peripheral Neuropathy in Breast Cancer Patients: A Pilot Study. Front Oncol. 2017 Jan 10;6:274.

Elektro-Akupunktur
1. Greenlee H, Crew KD, Capodice J, et al.: Randomized sham-controlled pilot trial of weekly electro-acupuncture for the prevention of taxane-induced peripheral neuropathy in women with early stage breast cancer. Breast Cancer Res Treat. 2016 Apr;156(3):453-464.

Medikamentöse Prävention

Venlafaxin
1. Aziz MT, Good BL, Lowe DK. Serotonin-norepinephrine reuptake inhibitors for the management of chemotherapy-induced peripheral neuropathy. Ann Pharmacother. 2014 May;48(5):626-32.
2. Durand JP, Deplanque G, Montheil V, et al.: Efficacy of venlafaxine for the prevention and relief of oxaliplatin-induced acute neurotoxicity: results of EFFOX, a randomized, double-blind, placebo-controlled phase III trial. Ann Oncol. 2012 Jan;23(1):200-5
3. Gallagher HC, Gallagher RM, Butler M, et al.: Venlafaxine for neuropathic pain in adults. Cochrane Database Syst Rev. 2015 Aug 23;(8):CD011091.

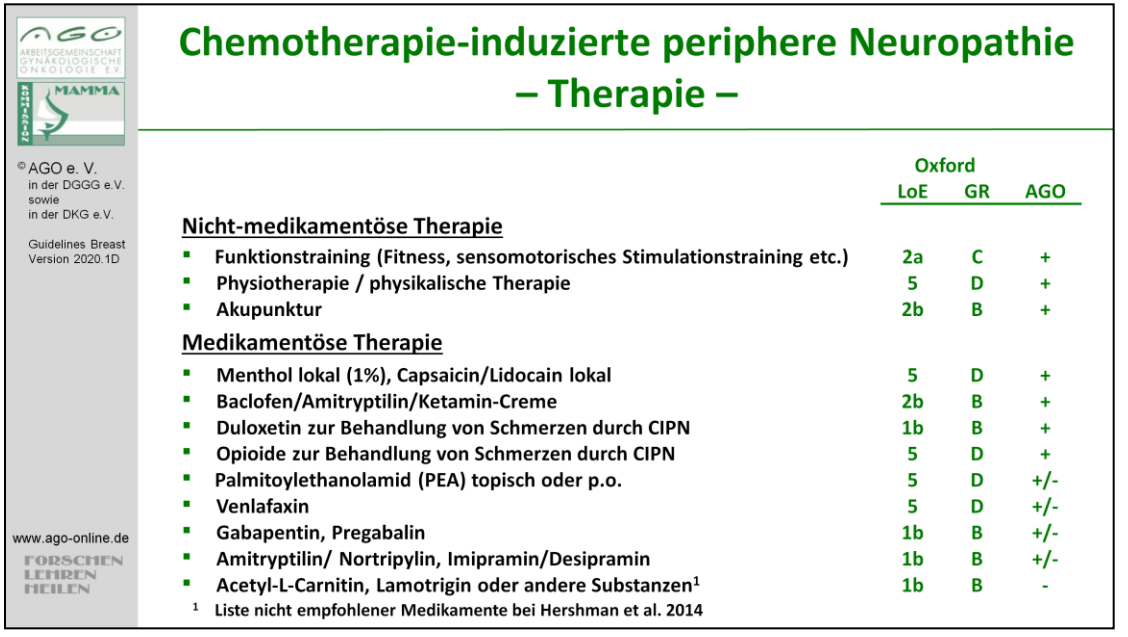
Palmitoylethanolamid (PEA)
1. Lombardi G, Miglio G, Varsaldi F, et al.: Oxyhomologation of the amide bond potentiates neuroprotective effects of the endolipid N-palmitoylethanolamine.
   J Pharmacol Exp Ther. 2007 Feb;320(2):599-606
2. Di Cesare Mannelli L, Pacini A, Corti F, et al.: Antineuropathic profile of N-palmitoylethanolamine in a rat model of oxaliplatin-induced neurotoxicity. PLoS One. 2015 Jun 3;10(6):e0128080.
3. Di Cesare Mannelli L, D'Agostino G, Pacini A, et al.: Palmitoylethanolamide is a disease-modifying agent in peripheral neuropathy: pain relief and neuroprotection share a PPAR-alpha-mediated mechanism. Mediators Inflamm. 2013;2013:328797

Verschiedene Substanzen
1. Schloss J, Colosimo M, Vitetta L. Herbal medicines and chemotherapy induced peripheral neuropathy (CIPN): A critical literature

review. Crit Rev Food Sci Nutr. 2017 Apr 13;57(6):1107-1118.
2. Schloss JM, Colosimo M, Airey C, et al.: Nutraceuticals and chemotherapy induced peripheral neuropathy (CIPN): a systematic review. Clin Nutr. 2013 Dec;32(6):888-93.
3. Kuriyama A, Endo K. Goshajinkigan for prevention of chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis. Support Care Cancer. 2017 Dec 26.
4. Kautio AL, Haanpää M, Leminen A, et al.: Amitriptyline in the prevention of chemotherapy-induced neuropathic symptoms. Anticancer Res. 2009 Jul;29(7):2601-6.
5. Schloss JM, Colosimo M, Airey C, et al.: A randomised, placebo-controlled trial assessing the efficacy of an oral B group vitamin in preventing the development of chemotherapy-induced peripheral neuropathy (CIPN). Support Care Cancer. 2017 Jan;25(1):195-204.
6. Leal AD, Qin R, Atherton PJ, et al.: Alliance for Clinical Trials in Oncology. North Central Cancer Treatment Group/Alliance trial N08CA-the use of glutathione for prevention of paclitaxel/carboplatin-induced peripheral neuropathy: a phase 3 randomized, double-blind, placebo-controlled study. Cancer. 2014 Jun 15;120(12):1890-7
7. Memeo A, Loiero M. Thioctic acid and acetyl-L-carnitine in the treatment of sciatic pain caused by a herniated disc: a randomized, double-blind, comparative study. Clin Drug Investig. 2008;28(8):495-500.

Acetyl-L-Carnitin

1. Hershman DL, Unger JM, Crew KD, et al.: Randomized double-blind placebo-controlled trial of acetyl-L-carnitine for the prevention of taxane-induced neuropathy in women undergoing adjuvant breast cancer therapy. J Clin Oncol. 2013 Jul 10;31(20):2627-33.
2. Hershman DL, Unger JM, Crew KD, et al.: Two-Year Trends of Taxane-Induced Neuropathy in Women Enrolled in a Randomized Trial of Acetyl-L-Carnitine (SWOG S0715). J Natl Cancer Inst. 2018 Jan 18.



Reviews / Leitlinien

1. Hershman DL, Lacchetti C, Dworkin RH, et al.: American Society of Clinical Oncology. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014 Jun 20;32(18):1941-67.
2. Hu LY, Mi WL, Wu GC, et al.: Prevention and Treatment for Chemotherapy-Induced Peripheral Neuropathy: Therapies Based on CIPN Mechanisms. Current Neuropharmacology, 2018, 16, 1-12
3. Majithia N, Temkin SM, Ruddy KJ, et al.: National Cancer Institute-supported chemotherapy-induced peripheral neuropathy trials: outcomes and lessons. Support Care Cancer. 2016 Mar;24(3):1439-47. doi: 10.1007/s00520-015-3063-4. Epub 2015 Dec 19.
4. Greenlee H, Hershman DL, Shi Z, et al.:BMI, Lifestyle Factors and Taxane-Induced Neuropathy in Breast Cancer Patients: The Pathways Study. J Natl Cancer Inst. 2016 Oct 28;109(2). pii: djw206. Print 2017 Feb.
5. Majithia N, Loprinzi CL, Smith TJ. New Practical Approaches to Chemotherapy-Induced Neuropathic Pain: Prevention, Assessment, and Treatment. Oncology (Williston Park). 2016 Nov 15;30(11):1020-9. Review.
6. Pachman DR, Barton DL, Watson JC, et al.: Chemotherapy-induced peripheral neuropathy: prevention and treatment. Clin Pharmacol Ther. 2011 Sep;90(3):377-87.
7. Schuler U, Heller S. :Chemotherapy-induced peripheral neuropathy and neuropathic pain. Schmerz. 2017 Aug;31(4):413-425.
8. Smith, E. M., H. Pang, C. Cirrincione, et al. (2013). "Effect of duloxetine on pain, function, and quality of life among patients with

chemotherapy-induced painful peripheral neuropathy: a randomized clinical trial." JAMA 309(13): 1359-1367.
9. Cliff J, Jorgensen AL, Lord R, et al.: The molecular genetics of chemotherapy-induced peripheral neuropathy: A systematic review and meta-analysis. Crit Rev Oncol Hematol. 2017 Dec;120:127-140.

Nicht-medikamentöse Therapie

Funktionstraining

1. Duregon F, Vendramin B, Bullo V, et al.: Effects of exercise on cancer patients suffering chemotherapy-induced peripheral neuropathy undergoing treatment: A systematic review. Crit Rev Oncol Hematol. 2018 Jan;121:90-100.
2. Smith TJ, Razzak AR, Blackford AL, Ensminger J, Saiki C, Longo-Schoberlein D, Loprinzi CL: A pilot randomized sham-controlled trial of mc5-a scrambler therapy in the treatment of chronic chemotherapy-induced peripheral neuropathy (cipn). Journal of palliative care 2020;35:53-58.
3. D'Alessandro EG, Nebuloni Nagy DR, de Brito CMM, et al.: Acupuncture for chemotherapy-induced peripheral neuropathy: A randomised controlled pilot study. BMJ Support Palliat Care 2019.
4. Lu W, Giobbie-Hurder A, Freedman RA, Shin IH, et al.: Acupuncture for chemotherapy-induced peripheral neuropathy in breast cancer survivors: A randomized controlled pilot trial. Oncologist 2019.

Medikamentöse Therapie

Menthol / Capsaicin

1. Fallon MT, Storey DJ, Krishan A, et al.: Cancer treatment-related neuropathic pain: proof of concept study with menthol--a TRPM8 agonist. Support Care Cancer. 2015 Sep;23(9):2769-77
2. Derry S, Rice AS, Cole P, et al.: Topical capsaicin (high concentration) for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2017 Jan 13;1:CD007393
3. Moon JY, Lee PB, Kim YC, et al.: Efficacy and Safety of 0.625% and 1.25% Capsaicin Patch in Peripheral Neuropathic Pain: Multi-Center, Randomized, and Semi-Double Blind Controlled Study. Pain Physician. 2017 Feb;20(2):27-35.

4. Simpson DM, Robinson-Papp J, Van J, et al.: Capsaicin 8% Patch in Painful Diabetic Peripheral Neuropathy: A Randomized, Double-Blind, Placebo-Controlled Study. J Pain. 2017 Jan;18(1):42-53
5. Anand P. Capsaicin and menthol in the treatment of itch and pain: recently cloned receptors provide the key. Gut. 2003 Sep;52(9):1233-5.

Baclofen/Amitryptilin/Ketamin-Creme
1. Barton DL, Wos EJ, Qin R, et al.: A double-blind, placebo-controlled trial of a topical treatment for chemotherapy-induced peripheral neuropathy: NCCTG trial N06CA. Support Care Cancer. 2011 Jun;19(6):833-41.
2. Pachman DR, Barton DL, Watson JC, et al.: Chemotherapy-induced peripheral neuropathy: prevention and treatment. Clin Pharmacol Ther. 2011 Sep;90(3):377-87.

Duloxetin
1. Smith EM, Pang H, Cirrincione C, et al.: Alliance for Clinical Trials in Oncology. Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced painful peripheral neuropathy: a randomized clinical trial. JAMA. 2013 Apr 3;309(13):1359-67

Akupunktur:

1. Han X, Wang L, Shi H, *et al.* Acupuncture combined with methylcobalamin for the treatment of chemotherapy- induced peripheral neuropathy in patients with multiple myeloma. *BMC Cancer* 2017;17:40.

2. Lu W, Giobbie-Hurder A, Freedman R, *et al.* Acupuncture for Chemotherapy-Induced Peripheral Neuropathy in Breast Cancer Survivors: A Randomized Controlled Pilot Trial. Oncologist. 2019 Oct 14:1-9 .

Palmitoylethanolamid (PEA)
1. Lombardi G, Miglio G, Varsaldi F, et al.: Oxyhomologation of the amide bond potentiates neuroprotective effects of the endolipid N-palmitoylethanolamine.
J Pharmacol Exp Ther. 2007 Feb;320(2):599-606

2. Di Cesare Mannelli L, Pacini A, Corti F, et al.: Antineuropathic profile of N-palmitoylethanolamine in a rat model of oxaliplatin-induced neurotoxicity. PLoS One. 2015 Jun 3;10(6):e0128080.
3. Di Cesare Mannelli L, D'Agostino G, Pacini A, et al.: Palmitoylethanolamide is a disease-modifying agent in peripheral neuropathy: pain relief and neuroprotection share a PPAR-alpha-mediated mechanism. Mediators Inflamm. 2013;2013:328797
4. Petrosino S, Di Marzo V. The pharmacology of palmitoylethanolamide and first data on the therapeutic efficacy of some of its new formulations. Br J Pharmacol. 2017 Jun;174(11):1349-1365.

Venlafaxin

1. Aziz MT, Good BL, Lowe DK. Serotonin-norepinephrine reuptake inhibitors for the management of chemotherapy-induced peripheral neuropathy. Ann Pharmacother. 2014 May;48(5):626-32.
2. Durand JP, Deplanque G, Montheil V, et al.: Efficacy of venlafaxine for the prevention and relief of oxaliplatin-induced acute neurotoxicity: results of EFFOX, a randomized, double-blind, placebo-controlled phase III trial. Ann Oncol. 2012 Jan;23(1):200-5
3. Gallagher HC, Gallagher RM, Butler M, et al.: Venlafaxine for neuropathic pain in adults. Cochrane Database Syst Rev. 2015 Aug 23;(8):CD011091.

Gabapentin, Pregabalin:

1. Rao RD, Michalak JC, Sloan Jaet al.: Efficacy of gabapentin in the management of chemotherapy-induced peripheral neuropathy: a phase 3 randomized, double-blind, placebo-controlled, crossover trial (N00C3). Cancer. 2007 Nov 1;110(9):2110-8.
2. Nishikawa T, Hasegawa K, Shintani D, et al.: Combination Therapy of Pregabalin with Tramadol for Treatment of Peripheral Neuropathy in Patients with Gynecological Cancer Receiving Taxane Containing Chemotherapy. Gan To Kagaku Ryoho. 2017 Mar;44(3):227-231.

Amitryptilin/Nortriptylin

1. Kautio AL, Haanpää M, Saarto T, et al.: Amitriptyline in the treatment of chemotherapy-induced neuropathic symptoms. J Pain Symptom Manage. 2008 Jan;35(1):31-9.
2. Hammack JE, Michalak JC, Loprinzi CL, et al.: Phase III evaluation of nortriptyline for alleviation of symptoms of cis-platinum-induced peripheral neuropathy. Pain. 2002 Jul;98(1-2):195-203.

Acetyl-L-Carnitin, Lamotrigin oder andere Substanzen:

1. Rao RD, Flynn PJ, Sloan JA, et al.: Efficacy of lamotrigine in the management of chemotherapy-induced peripheral neuropathy: a phase 3 randomized, double-blind, placebo-controlled trial, N01C3. Cancer. 2008 Jun 15;112(12):2802-8
2. Schloss J, Colosimo M, Vitetta L. Herbal medicines and chemotherapy induced peripheral neuropathy (CIPN): A critical literature review. Crit Rev Food Sci Nutr. 2017 Apr 13;57(6):1107-1118.
3. Schloss JM, Colosimo M, Airey C, et al.: Nutraceuticals and chemotherapy induced peripheral neuropathy (CIPN): a systematic review. Clin Nutr. 2013 Dec;32(6):888-93.
4. Kuriyama A, Endo K. Goshajinkigan for prevention of chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis. Support Care Cancer. 2017 Dec 26.
5. Kautio AL, Haanpää M, Leminen A, et al.: Amitriptyline in the prevention of chemotherapy-induced neuropathic symptoms. Anticancer Res. 2009 Jul;29(7):2601-6.
6. Schloss JM, Colosimo M, Airey C, et al.: A randomised, placebo-controlled trial assessing the efficacy of an oral B group vitamin in preventing the development of chemotherapy-induced peripheral neuropathy (CIPN). Support Care Cancer. 2017 Jan;25(1):195-204.
7. Leal AD, Qin R, Atherton PJ, Haluska P, et al.: Alliance for Clinical Trials in Oncology. North Central Cancer Treatment Group/Alliance trial N08CA-the use of glutathione for prevention of paclitaxel/carboplatin-induced peripheral neuropathy: a phase 3 randomized, double-blind, placebo-controlled study. Cancer. 2014 Jun 15;120(12):1890-7
8. Memeo A, Loiero M. Thioctic acid and acetyl-L-carnitine in the treatment of sciatic pain caused by a herniated disc: a randomized, double-blind, comparative study. Clin Drug Investig. 2008;28(8):495-500.
9. Hershman DL, Unger JM, Crew KD, et al.: Randomized double-blind placebo-controlled trial of acetyl-L-carnitine for the prevention of taxane-induced neuropathy in women undergoing adjuvant breast cancer therapy. J Clin Oncol. 2013 Jul 10;31(20):2627-33.
10. Hershman DL, Unger JM, Crew KD, et al.: Two-Year Trends of Taxane-Induced Neuropathy in Women Enrolled in a Randomized Trial of Acetyl-L-Carnitine (SWOG S0715). J Natl Cancer Inst. 2018 Jan 18.
11. Schloss JM, Colosimo M, Airey C, et al.: Nutraceuticals and chemotherapy induced peripheral neuropathy (CIPN): a systematic review. Clin Nutr. 2013 Dec;32(6):888-93.
12. Schloss J, Colosimo M, Vitetta L. Herbal medicines and chemotherapy induced peripheral neuropathy (CIPN): A critical literature review. Crit Rev Food Sci Nutr. 2017 Apr 13;57(6):1107-1118.
13. Duregon F, Vendramin B, Bullo V, et al.: Effects of exercise on cancer patients suffering chemotherapy-induced peripheral neuropathy undergoing treatment: A systematic review. Crit Rev Oncol Hematol. 2018 Jan;121:90-100.
14. The prescription of medical cannabis by a transitional pain service to wean a patient with complex pain from opioid use following liver transplantation: a case report.

15. Meng H, Hanlon JG, Katznelson R, et al. Can J Anaesth. 2016 Mar;63(3):307-10.
16. Lynch ME, Cesar-Rittenberg P, Hohmann AG. A double-blind, placebo-controlled, crossover pilot trial with extension using an oral mucosal cannabinoid extract for treatment of chemotherapy-induced neuropathic pain. J Pain Symptom Manage. 2014 Jan;47(1):166-73.
17. Hu LY, Mi WL, Wu GC, et al.: Prevention and Treatment for Chemotherapy-Induced Peripheral Neuropathy: Therapies Based on CIPN Mechanisms. Current Neuropharmacology, 2018, 16, 1-12
18. Hershman DL, Lacchetti C, Dworkin RH, et al.: Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014 Jun 20;32(18):1941-67.
19. Majithia N, Temkin SM, Ruddy KJ, et al.: National Cancer Institute-supported chemotherapy-induced peripheral neuropathy trials: outcomes and lessons. Support Care Cancer. 2016 Mar;24(3):1439-47.

Nebenwirkungen nach Organsystemen
Inzidenz, Prävention, Therapie

Guidelines Breast
Version 2020.1D

7. Herzerkrankungen

Statements

"Equivalent cardiotoxicity of doxorubicin and epirubicin at recommended dose levels (450–500 and 900–1000 mg/m² cum. dose, resp.)"

"Liposome encapsulated anthracyclines (doxorubicin) induce less cardiotoxicity"

1. van Dalen EC Different anthracycline derivates for reducing cardiotoxicity in cancer patients. Cochrane Database Syst Rev. 2010 Mar 17;(3):CD005006. Review. Update in: Cochrane Database Syst Rev. 2010;(5):CD005006.

"Anthracycline- or trastuzumab-associated cardiotoxicity may occur earlier/more frequently…"

1. Petrelli F: 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
2. Azim HA Jr, de Azambuja E, Colozza M,et al.: Long-term toxic effects of adjuvant chemotherapy in breast cancer. Ann Oncol. 2011 Sep;22(9):1939-47.

"Trastuzumab-related cardiotoxicity in the elderly: a role for cardiovascular risk factors."

1. Serrano C, Cortés J, De Mattos-Arruda L, et al.: Trastuzumab-related cardiotoxicity in the elderly: a role for cardiovascular risk factors. Ann Oncol. 2011 Aug 9.

2. de Azambuja E, Ponde N, Procter M, et al: A pooled analysis of the cardiac events in the trastuzumab adjuvant trials. Breast Cancer Res Treat 2019.
3. Kabore EG, Guenancia C, Vaz-Luis I, et al: Association of body mass index and cardiotoxicity related to anthracyclines and trastuzumab in early breast cancer: French canto cohort study. PLoS medicine 2019;16:e1002989.
4. Leemasawat K, Phrommintikul A, Chattipakorn SC, Chattipakorn N: Mechanisms and potential interventions associated with the cardiotoxicity of erbb2-targeted drugs: Insights from in vitro, in vivo, and clinical studies in breast cancer patients. Cell Mol Life Sci 2019.
5. Tarantini L, Gori S, Faggiano P, et al.: ICARO (Italian CARdio-Oncologic) Network. Adjuvant trastuzumab cardiotoxicity in patients over 60 years of age with early breast cancer: a multicenter cohort analysis. Ann Oncol. 2012 Dec;23(12):3058-63.
6. Sautter-Bihl ML, Souchon R, Gerber B: Adjuvant therapy for women over age 65 with breast cancer. Dtsch Arztebl Int 108:365-371, 2011

*"*Monitoring of cardiac function before / during / after treatment: Echocardiography (LVEF or SF in %)"

1. Ewer MS, Ewer SM. Cardiotoxicity of anticancer treatments: what the cardiologist needs to know. Nat Rev Cardiol. 2010 Oct;7(10):564-75. Review.
2. Slamon D: Breast Cancer International Research Group. Adjuvant trastuzumab in HER2-positive breast cancer. N Engl J Med. 2011 Oct 6;365(14):1273-83
3. Verma S: Is cardiotoxicity being adequately assessed in current trials of cytotoxic and targeted agents in breast cancer? Ann Oncol. 2011 May;22(5):1011-8. Epub 2010 Nov 22..
4. Lluch A: Anthracycline cardiotoxicity in the elderly cancer patient: a SIOG expert position paper. Aapro M, Bernard-Marty C, Brain EG, Batist G, Erdkamp F, Krzemieniecki K, Leonard R. Ann Oncol. 2011;22:257-67.
5. Costa RB: Efficacy and cardiac safety of adjuvant trastuzumab-based chemotherapy regimens for HER2-positive early breast cancer. Ann Oncol. 2010 Nov;21(11):2153-60.
6. Yancy CW, Jessup M, Bozkurt B, et al. 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Card Fail. 2016 Sep;22(9):659-69. doi: 10.1016/j.cardfail.2016.07.001. Epub 2016 Jul 6.
7. Smith LA, Cornelius VR, Plummer CJ, et al.: Cardiotoxicity of anthracycline agents for the treatment of cancer: systematic review and meta-analysis of randomised controlled trials. BMC Cancer. 2010 Jun 29;10:337. doi: 10.1186/1471-2407-10-337.

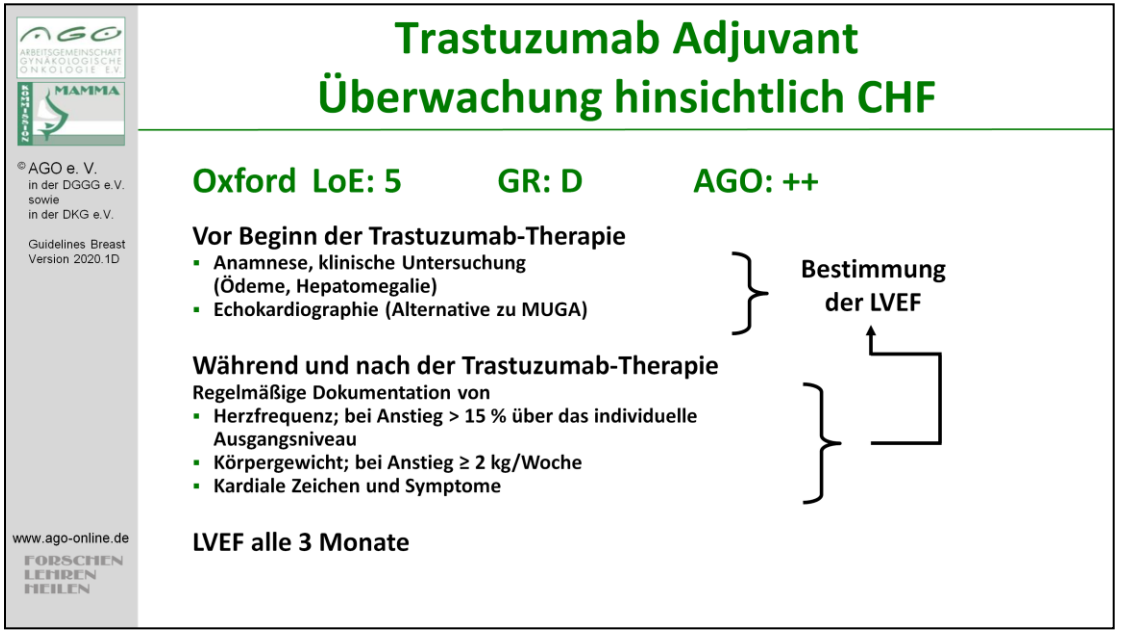
8. Drafts BC, Twomley KM, D'Agostino R Jr, et al. Low to moderate dose anthracycline-based chemotherapy is associated with early noninvasive imaging evidence of subclinical cardiovascular disease. JACC Cardiovasc Imaging. 2013 Aug;6(8):877-85. doi: 10.1016/j.jcmg.2012.11.017. Epub 2013 May 1.
9. Adamo V, Ricciardi GR, Adamo B, et al.: The risk of toxicities from trastuzumab, alone or in combination, in an elderly breast cancer population. Oncology. 2014;86(1):16-21. doi: 10.1159/000353450. Epub 2013 Dec 10
10. NCCN (National Comprehensive Cancer Network , 2016): http://www.nccn.org
11. 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.
12. Lorenzini C, Lamberti C, Aquilina M, et al.: Reliability of Left Ventricular Ejection Fraction from Three-Dimensional Echocardiography for Cardiotoxicity Onset Detection in Patients with Breast Cancer. J Am Soc Echocardiogr. 2017 Nov;30(11):1103-1110.

Troponin as Early Predictor for Cardiotoxicity

1. Ponde N, Bradbury I, Lambertini M, et al. Cardiac biomarkers for early detection and prediction of trastuzumab and/or lapatinib-induced cardiotoxicity in patients with HER2-positive early-stage breast cancer: a NeoALTTO sub-study (BIG 1-06). Breast Cancer Res Treat. 2017 Dec 27.
2. Kitayama H, Kondo T, Sugiyama J, et al.: High-sensitive troponin T assay can predict anthracycline- and trastuzumab-induced cardiotoxicity in breast cancer patients. Breast Cancer. 2017 Nov;24(6):774-782.

Betablocker-Prophylaxe

1. Gujral DM, Lloyd G, Bhattacharyya S. Effect of prophylactic betablocker or ACE inhibitor on cardiac dysfunction & heart failure during anthracycline chemotherapy ± trastuzumab. Breast. 2018 Feb;37:64-71.
2. Oliva S, Cioffi G, Frattini S, et al.: Administration of angiotensin-converting enzyme inhibitors and β-blockers during adjuvant trastuzumab chemotherapy for nonmetastatic breast cancer: marker of risk or cardioprotection in the real world? Oncologist. 2012;17(7):917-24.
3. Kalam K, Marwick TH. Role of cardioprotective therapy for prevention of cardiotoxicity with chemotherapy: a systematic review and meta-analysis. Eur J Cancer. 2013 Sep;49(13):2900-9.



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

1. Perez EA, Suman VJ, Davidson NE, et al.: Cardiac safety analysis of doxorubicin and cyclophosphamide followed by paclitaxel with or without trastuzumab in the North Central Cancer Treatment Group N9831 adjuvant breast cancer trial. J Clin Oncol. 2008 Mar 10;26(8):1231-8. Epub 2008 Feb 4.
2. Mackey JR, Clemons M, Côté MA, et al.: Cardiac management during adjuvant trastuzumab therapy: recommendations of the Canadian Trastuzumab Working Group.
3. Curr Oncol. 2008 Feb;15(1):24-35.

"Trastuzumab simultaneous to radiotherapy"

1. Halyard MY, Pisansky TM, Dueck AC: Radiotherapy and adjuvant trastuzumab in operable breast cancer: tolerability and adverse event data from the NCCTG Phase III Trial N9831.J Clin Oncol 27: 2638-2644, 2009
2. Viani GA, Afonso SL, Stefano EJ, et al.: Adjuvant trastuzumab in the treatment of Her2 positive early breast cancer: a metaanalysis of published randomized trials. BMC Cancer 2007; 7:153-164
3. Kroeze SG, Fritz C, Hoyer M, et al.: Toxicity of concurrent stereotactic radiotherapy and targeted therapy or immunotherapy: A systematic review. Cancer Treat Rev. 2016 Dec 19;53:25-37. doi: 10.1016/j.ctrv.2016.11.013. [Epub ahead of print]

"Trastuzumab simultaneous to epirubicin"

1. Untch M, Muscholl M, Tjulandin S, et al.: First-line trastuzumab plus epirubicin and cyclophosphamide therapy in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer: cardiac safety and efficacy data from the Herceptin, Cyclophosphamide, and Epirubicin (HERCULES) trial. J Clin Oncol. 2010 Mar 20;28(9):1473-80.
2. Untch M, Rezai M, Loibl S, et al.: Neoadjuvant treatment with trastuzumab in HER2-positive breast cancer: results from the GeparQuattro study. J Clin Oncol. 2010 Apr 20;28(12):2024-31.
3. van Ramshorst MS, van Werkhoven E, Honkoop AH, et al.: Toxicity of dual HER2-blockade with pertuzumab added to anthracycline versus non-anthracycline containing chemotherapy as neoadjuvant treatment in HER2-positive breast cancer: The

TRAIN-2 study. Breast. 2016 Oct;29:153-9. doi: 10.1016/j.breast.2016.07.017. Epub 2016 Aug 5.

"Trastuzumab simultaneous to doxorubicin"

1. Slamon D, Eiermann W, Robert N, et al.: Adjuvant trastuzumab in HER2-positive breast cancer. N Engl J Med. 2011 Oct 6;365(14):1273-83

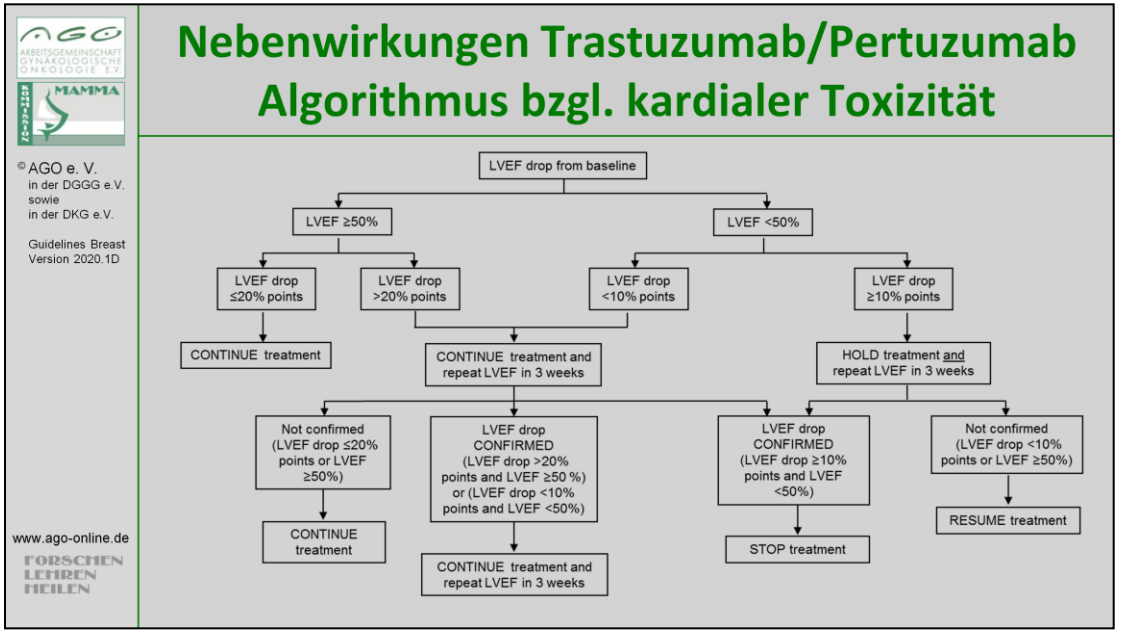
"Anthracycline simultaneous to radiotherapy"

1. Toledano A, Garaud P, Serin D, et al.: Concurrent administration of adjuvant chemotherapy and radiotherapy after breast-conserving surgery enhances late toxicities: long-term results of the ARCOSEIN multicenter randomized study. Int J Radiation Oncology Biol. Phys. 2006; 65: 324-332.

"Tamoxifen simultaneous to radiotherapy"

1. Kraus-Tiefenbacher U, Sfintizky A, Welzel G, et al.: Factors of influence on acute skin toxicity of breast cancer patients treated with standard external beam radiotherapy (EBRT) after breast conserving surgery (BCS). Radiat Oncol. 2012 Dec 18;7(1):217. [Epub ahead of print]
2. Varga Z, Cserháti A, Kelemen G, et al.: Role of systemic therapy in the development of lung sequelae after conformal radiotherapy in breast cancer patients. Int J Radiat Oncol Biol Phys. 2011 Jul 15;80(4):1109-16.
3. Hoeller U, Borgmann K, Feyer P, et al.: On the interaction of adjuvant radiotherapy and tamoxifen treatment for breast cancer. Strahlenther Onkol. 2007 Oct;183(10):535-44.
4. Munshi A, Gupta D. Concurrent versus sequential radiotherapy and tamoxifen in breast cancer - The CONSET trial is launched. Acta Oncol. 2011 Jan;50(1):154-5.

1. Valakh V, Trombetta MG, Werts ED, et al.: Influence of concurrent anastrozole on acute and late side effects of whole breast radiotherapy. Am J Clin Oncol. 2011 Jun;34(3):245-8.
2. Telli ML, Hunt SA, Carlson RW, et al.: Trastuzumab-Related Cardiotoxicity: Calling Into Question the Concept of Reversibility. Journal of Clin Oncol, 2007; 25: 3525-3533
3. Viani GA, Afonso SL, Stefano EJ, et al.: Adjuvant trastuzumab in the treatment of Her2 positive early breast cancer: a metaanalysis of published randomized trials. BMC Cancer 2007; 7:153-164



1. Keefe DL: Trastuzumab-associated cardiotoxicity. Cancer 95:1592-1600, 2002
2. Zeglinski M, Ludke A, Jassal DS, et al.: Trastuzumab-induced cardiac dysfunction: A 'dual-hit'. Exp Clin Cardiol. 2011 Fall;16(3):70-4.
3. Popat S, Smith IE. Therapy Insight: anthracyclines and trastuzumab--the optimal management of cardiotoxic side effects. Nat Clin Pract Oncol. 2008 Jun;5(6):324-35.
4. Baselga J, Cortes J, Kim S-B et al. Pertuzumab plus Trastuzumab plus Docetaxel for metastatic breast cancer. N Engl J Med 2012; 366:109-119
5. Perez EA, Barrios C, Eiermann W, et al.: Trastuzumab Emtansine With or Without Pertuzumab Versus Trastuzumab Plus Taxane for Human Epidermal Growth Factor Receptor 2-Positive, Advanced Breast Cancer: Primary Results From the Phase III MARIANNE Study. J Clin Oncol. 2017 Jan 10;35(2):141-148. Epub 2016 Nov
6. Loibl S, Jackisch C, Schneeweiss A, et al.: investigators of the German Breast Group (GBG) and the Arbeitsgemeinschaft Gynäkologische Onkologie—Breast (AGO-B) study groups..Dual HER2-blockade with pertuzumab and trastuzumab in HER2-positive early breast cancer: a subanalysis of data from the randomized phase III GeparSepto trial. Ann Oncol. 2016 Nov 9.
7. Swain SM, Ewer MS, Cortés J, et al.: Cardiac tolerability of pertuzumab plus trastuzumab plus docetaxel in patients with HER2-positive metastatic breast cancer in CLEOPATRA: a randomized, double-blind, placebo-controlled phase III study. Oncologist. 2013;18(3):257-64. doi: 10.1634/theoncologist.2012-0448. Epub 2013 Mar 8.

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Guidelines Breast
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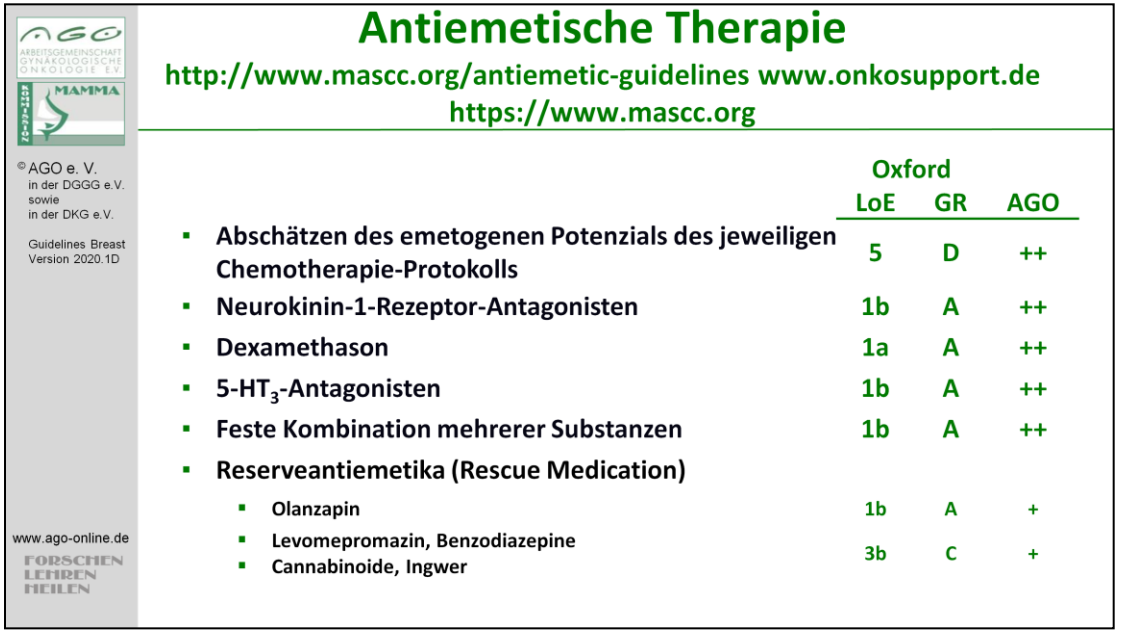
8. Erkrankungen des Gastrointestinaltrakts
   - Nausea, Emesis (Übelkeit, Erbrechen)
   - Mukositis
     - Stomatitis (Evrolimus)
   - Diarrhoe
   - Obstipation



1. Hesketh, Paul J, Kris MG, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol 2017;35(28):3240-61
2. Walsh D, Davis M, Ripamonti C, et al.: 2016 updated mascc/esmo consensus recommendations: Management of nausea and vomiting in advanced cancer. Support Care Cancer 2017;25:333-340.
3. Olver I, Ruhlmann CH, Jahn F, et al: 2016 updated mascc/esmo consensus recommendations: Controlling nausea and vomiting with chemotherapy of low or minimal emetic potential. Support Care Cancer 2017;25:297-301.
4. Razvi Y, Chan S, McFarlane T et al: Asco, nccn, mascc/esmo: A comparison of antiemetic guidelines for the treatment of chemotherapy-induced nausea and vomiting in adult patients. Support Care Cancer 2019;27:87-95.
5. Jordan K, Jahn F, Aapro M. Recent developments in the prevention of chemotherapy induced nausea and vomiting. Ann Oncol 2015;26:1081-90.
6. Hesketh PJ, Aaapro M, Jordan K et al. A review of NEPA, a novel fixed antiemetic combination with the potential for enhancing guideline adherence
and improving control of chemotherapy-induced nausea and vomiting. Biomed Res Int 2015;65:1879
7. Schwartzberg LS, Rugo HS, Aapro M. New and emerging therapeutic options for the management of chemotherapy-induced nausea and vomiting Clin Adv Hematol Oncol 2015;15(3 Suppl. 3):3-13
8. Jordan K, Schaffrath F, Jahn F et al. Neuropharmacology and management of chemotherapy-induced nausea and vomiting in

patients with breast cancer. Breast Care 2014;9:246-53
9. Navari RM, Qin R, Ruddy KJ, et al: Olanzapine for the prevention of chemotherapy-induced nausea and vomiting. N Engl J Med 2016;375:134-142.

10. Keith B. :Systematic review of the clinical effect of glucocorticoids on nonhematolic malignancy BMC Cancer (2008);8:84
11. Hesketh PJ, Younger J, Sanz-Altamira P, et al.: Aprepitant as salvage antiemetic therapy in breast cancer patients receiving doxorubicin and cyclophosphamide. Support Care Cancer. 2008 Dec 6. [Epub ahead of print]
12. Schmoll HJ et al. (2006) Comparison of an aprepitant regimen with a multiple-day ondansetron regimen, both with dexamethasone, for antiemetic efficacy in high-dose cisplatin treatment. Ann Oncol 17: 4112–4119
13. Hesketh PJ, Grunberg SM, Gralla RJ, et al.: Aprepitant Protocol 052 Study Group. The oral neurokinin-1 antagonist aprepitant for the prevention of chemotherapy-induced nausea and vomiting: a multinational, randomized, double-blind, placebo-controlled trial in patients receiving high-dose cisplatin--the Aprepitant Protocol 052 Study Group. J Clin Oncol. 2003 Nov 15;21(22):4112-9. Epub 2003 Oct 14
14. Poli-Bigelli S, Rodrigues-Pereira J, Carides AD, et al.: Aprepitant Protocol 054 Study Group. Addition of the neurokinin 1 receptor antagonist aprepitant to standard antiemetic therapy improves control of chemotherapy-induced nausea and vomiting. Results from a randomized, double-blind, placebo-controlled trial in Latin America. Cancer. 2003 Jun 15;97(12):3090-8.
15. Massa E, Astara G, Madeddu C, et al.: Palonosetron plus dexamethasone effectively prevents acute and delayed chemotherapy-induced nausea and vomiting following highly or moderately emetogenic chemotherapy in pre-treated patients who have failed to respond to a previous antiemetic treatment: Comparison between elderly and non-elderly patient response. Crit Rev Oncol Hematol. 2008 Aug 23. [Epub ahead of print
16. Grunberg SM, Dugan M, Muss H, et al.: Effectiveness of a single-day three-drug regimen of dexamethasone, palonosetron, and aprepitant for the prevention of acute and delayed nausea and vomiting caused by moderately emetogenic chemotherapy. Support Care Cancer. 2008 Nov 27. [Epub ahead of print]
17. Aapro MS, Grunberg SM, Manikhas GM, et al.: A phase III, double-blind, randomized trial of palonosetron compared with ondansetron in preventing chemotherapy-induced nausea and vomiting following highly emetogenic chemotherapy. Ann Oncol. 2006 Sep;17(9):1441-9. Epub 2006 Jun 9.
18. Navari RM, Madajewicz S, Anderson N, et al.: Oral ondansetron for the control of cisplatin-induced delayed emesis: a large, multicenter, double-blind, randomized comparative trial of ondansetron versus placebo. J Clin Oncol. 1995 Sep;13(9):2408-16.
19. Olver I, Paska W, Depierre A, et al.: A multicentre, double-blind study comparing placebo, ondansetron and ondansetron plus

dexamethasone for the control of cisplatin-induced delayed emesis. Ondansetron Delayed Emesis Study Group. Ann Oncol. 1996 Nov;7(9):945-52

Olanzepine:

1 Hironobu H, Masakazu A, Osamu Tokuyama, 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 Oncology December 11, 2019DOI:https://doi.org/10.1016/S1470-2045(19)30678-3

2 Slimano F, Netzer F, Borget I et al.:Olanzapine as antiemetic drug in oncology: a retrospective study in non-responders to standard antiemetic therapy. Int J Clin Pharm. 2018 Oct;40(5):1265-1271. doi: 10.1007/s11096-018-0649-1. Epub 2018 May 9.

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.

Antiemetische Therapie
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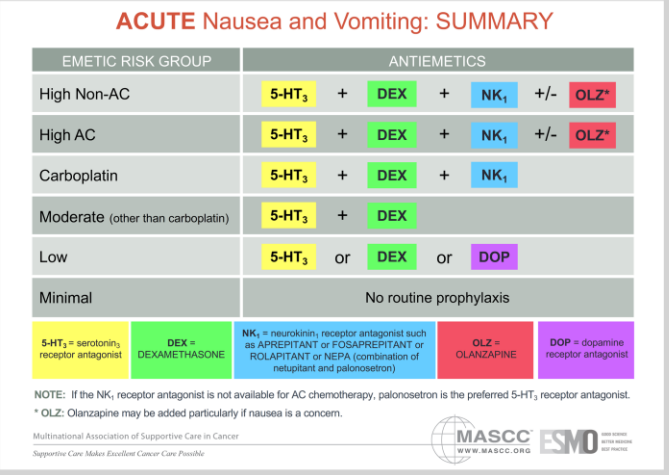

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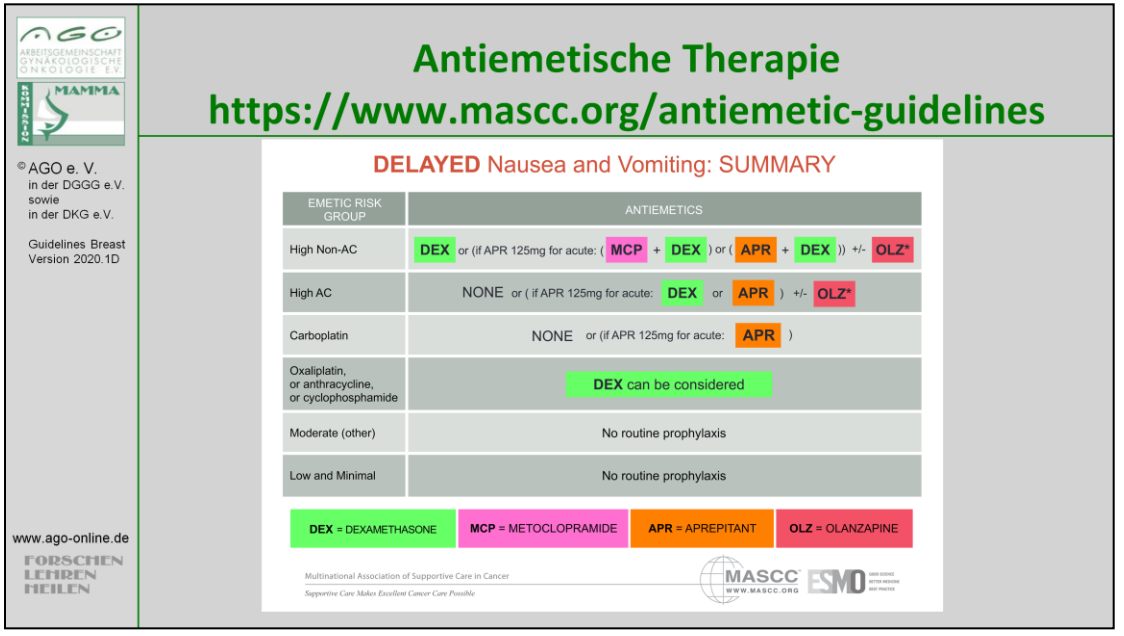

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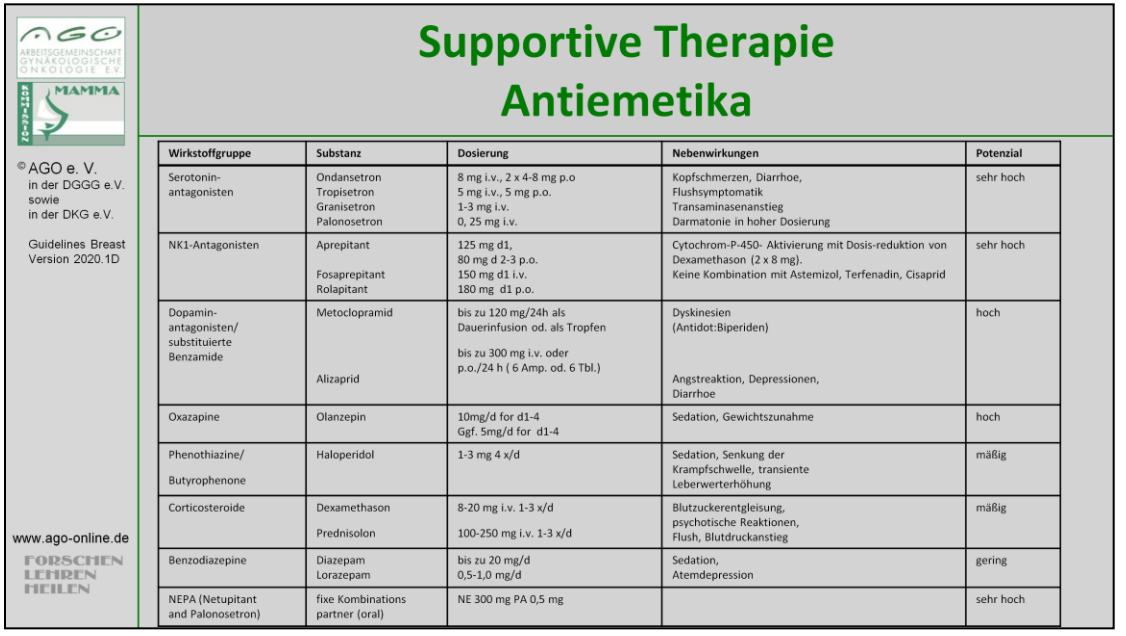
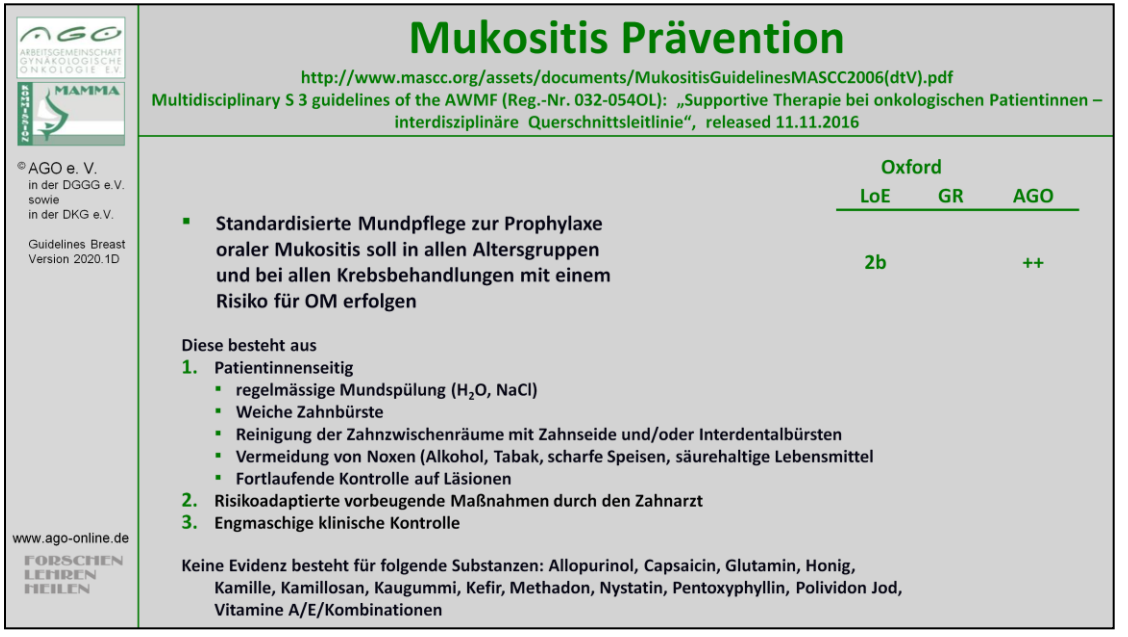


Wirkstoffgruppe	Substanz	Dosierung	Nebenwirkungen	Potenzial
Serotonin-antagonisten	Ondansetron Tropisetron Granisetron Palonosetron	8 mg i.v., 2 x 4-8 mg p.o 5 mg i.v., 5 mg p.o. 1-3 mg i.v. 0, 25 mg i.v.	Kopfschmerzen, Diarrhoe, Flushsymptomatik Transaminasenanstieg Darmatonie in hoher Dosierung	sehr 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, Gewichtszunahme	hoch
Phenothiazine/ Butyrophenone	Haloperidol	1-3 mg 4 x/d	Sedation, Senkung der Krampfschwelle, transiente Leberwerterhöhung	mäßig
Corticosteroide	Dexamethason Prednisolon	8-20 mg i.v. 1-3 x/d 100-250 mg i.v. 1-3 x/d	Blutzuckerentgleisung, psychotische Reaktionen, Flush, Blutdruckanstieg	mäßig
Benzodiazepine	Diazepam Lorazepam	bis zu 20 mg/d 0,5-1,0 mg/d	Sedation, Atemdepression	gering
NEPA (Netupitant and Palonosetron)	fixe Kombinations partner (oral)	NE 300 mg PA 0,5 mg		sehr hoch

Olanzapine:

1. Hironobu H, Masakazu A, Osamu Tokuyama, 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 Oncology December 11, 2019DOI:https://doi.org/10.1016/S1470-2045(19)30678-3
2. Slimano F, Netzer F, Borget I, et al.Olanzapine as antiemetic drug in oncology: a retrospective study in non-responders to standard antiemetic therapy. Int J Clin Pharm. 2018 Oct;40(5):1265-1271. doi: 10.1007/s11096-018-0649-1. Epub 2018 May 9.
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

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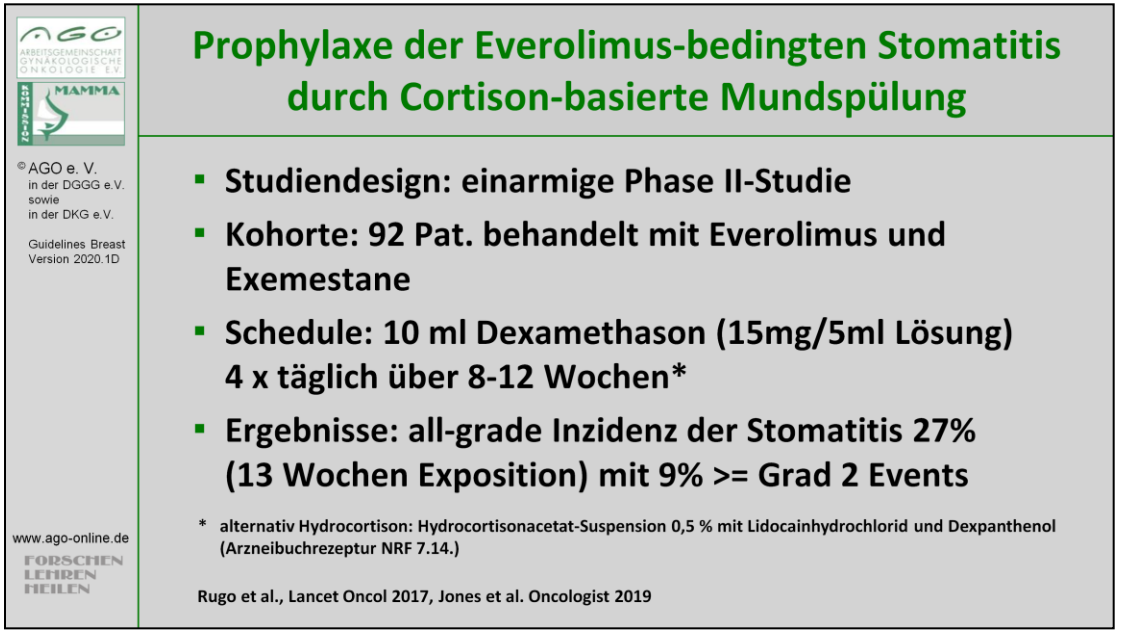
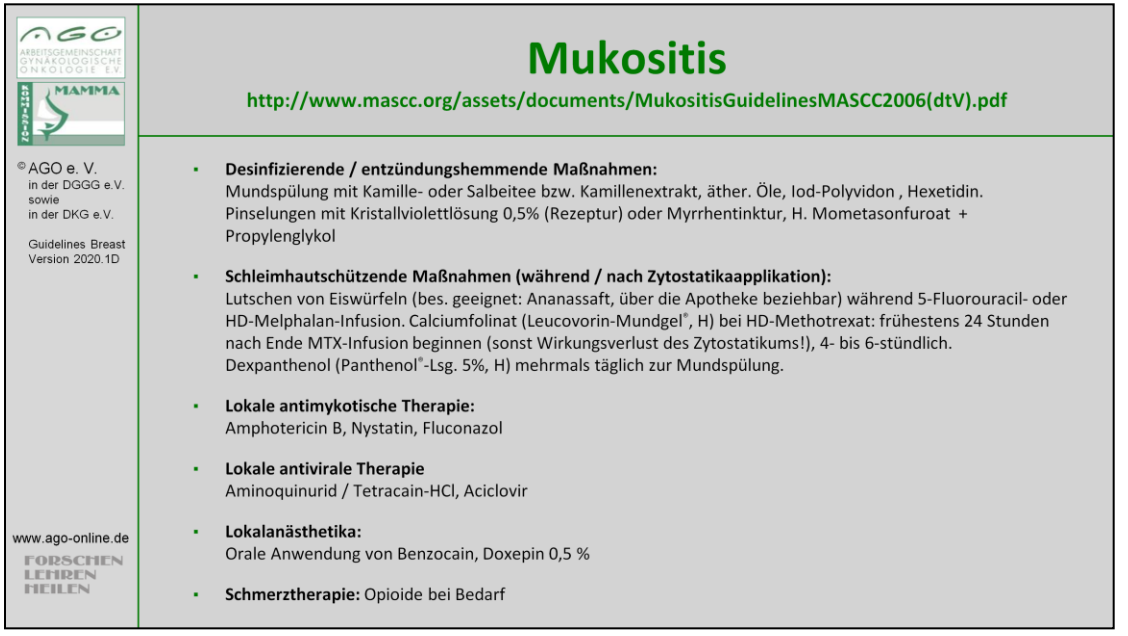
AWMF Registernummer: 032/054OL, http://leitlinienprogramm- onkologie.de/Supportive-Therapie.95.0.html (Zugriff am 08.01.2020)

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.



1. Rugo HS, Seneviratne L, Beck JT, et al: Prevention of everolimus-related stomatitis in women with hormone receptor-positive, her2-negative metastatic breast cancer using dexamethasone mouthwash (swish): A single-arm, phase 2 trial. Lancet Oncol 2017;18:654-662.
2. Jones VE, McIntyre KJ, Paul D, Wilks ST, et al.:Evaluation of miracle mouthwash plus hydrocortisone versus prednisolone mouth rinses as prophylaxis for everolimus-associated stomatitis: A randomized phase ii study. Oncologist 2019;24:1153-1158.



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1. http://www.mascc.org/assets/documents/MukositisGuidelinesMASCC2006(dtV).pdf
2. 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
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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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.
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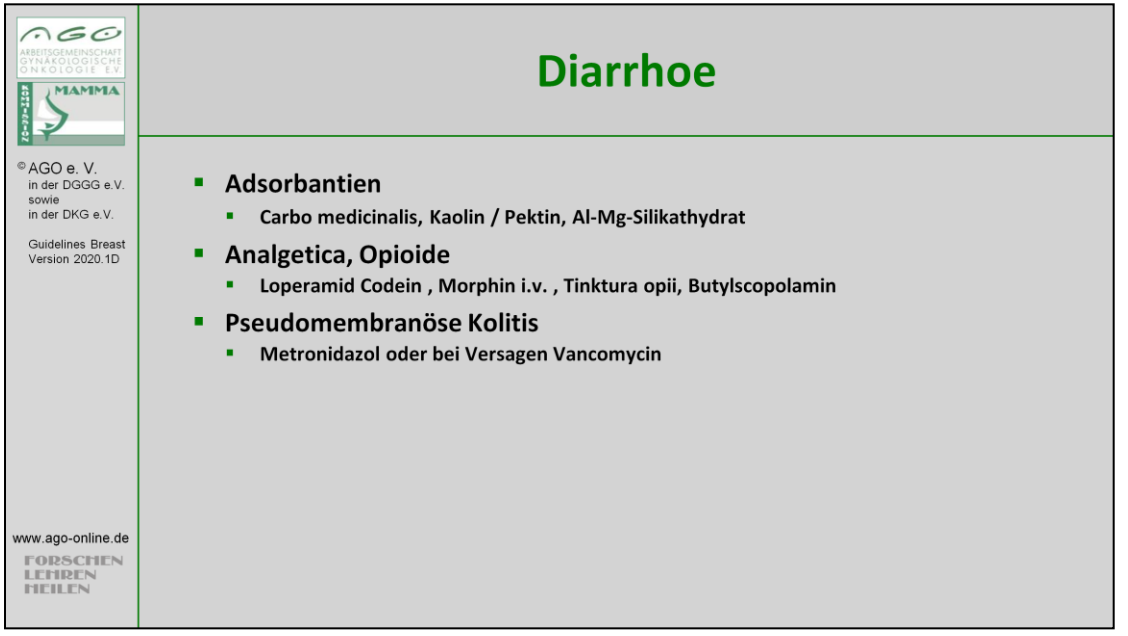

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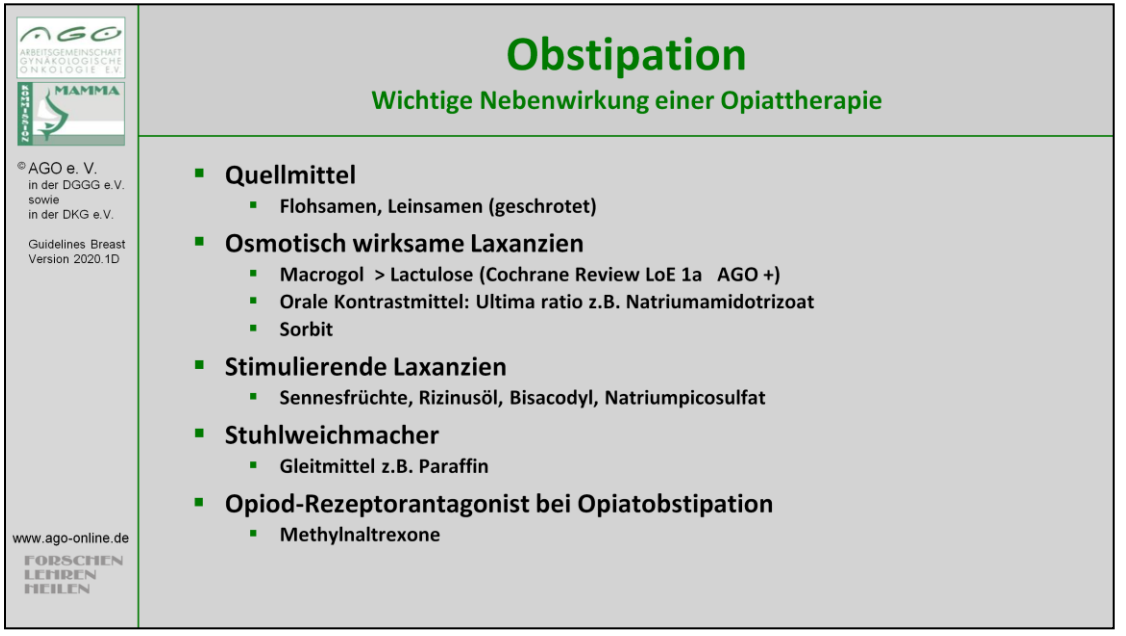
1. D. E. Peterson, C. B. Boers-Doets, R. J. Bensadoun, et al. on behalf of the ESMO Guidelines Committee Management of oral and gastrointestinal mucosal injury: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up Annals of Oncology 2015:26 (Supplement 5): v139–v151.
2. Stein A, Voigt W, Jordan K. Chemotherapy-induced diarrhea: pathophysiology, frequency and guideline-based management Ther Adv Med Oncol 2010:2(1) 51-63
3. Coyle, V. M., D. Lungulescu, C. Toganel, et al. (2013). "A randomised double-blind placebo-controlled phase II study of AGI004 for control of chemotherapy-induced diarrhoea." Br J Cancer 2013:108(5);1027-1033.
4. Hoff, P. M., D. F. Saragiotto, C. H. Barrios, et al. (2014). "Randomized Phase III Trial Exploring the Use of Long-Acting Release Octreotide in the Prevention of Chemotherapy-Induced Diarrhea in Patients With Colorectal Cancer: The LARCID Trial." J Clin Oncol 2014:32;1006-11

5. Kee, B. K., J. S. Morris, R. S. Slack, et al. "A phase II, randomized, double blind
6. trial of calcium aluminosilicate clay versus placebo for the prevention of diarrhea in patients with metastatic colorectal cancer treated with irinotecan." Support Care Cancer 2015:23;661-70.
7. Middleton, G., S. Brown, C. Lowe, T. et al. (2013). "A randomised phase III trial of the pharmacokinetic biomodulation of irinotecan using oral ciclosporin in advanced colorectal cancer: results of the Panitumumab, Irinotecan & Ciclosporin in COLOrectal cancer therapy trial (PICCOLO)." Eur J Cancer 2013, 49(16): 3507-3516.



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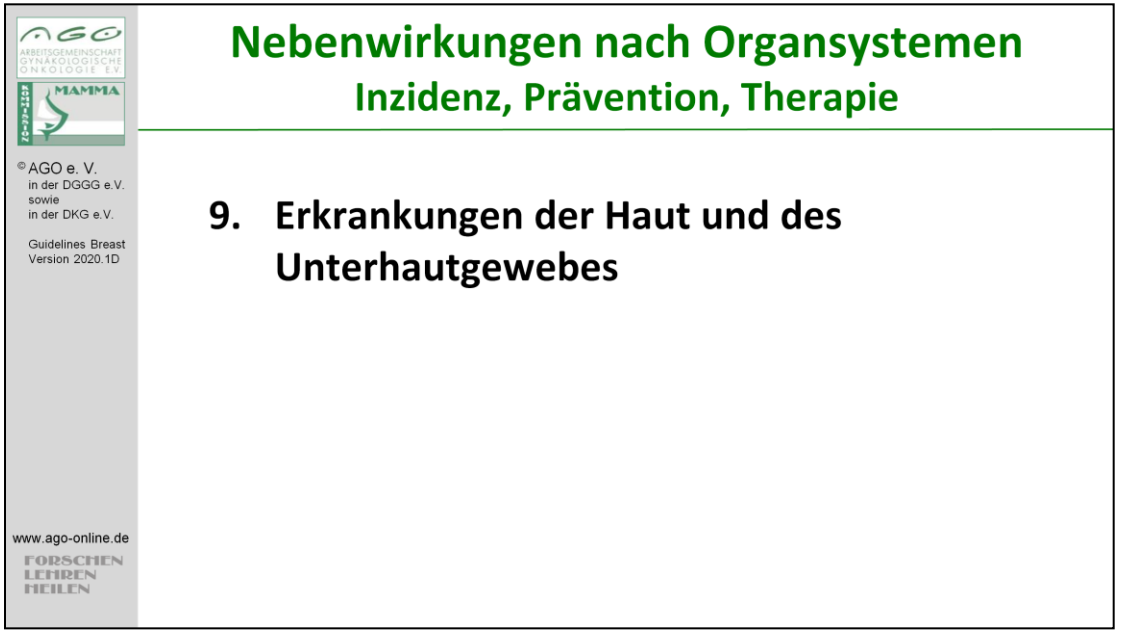

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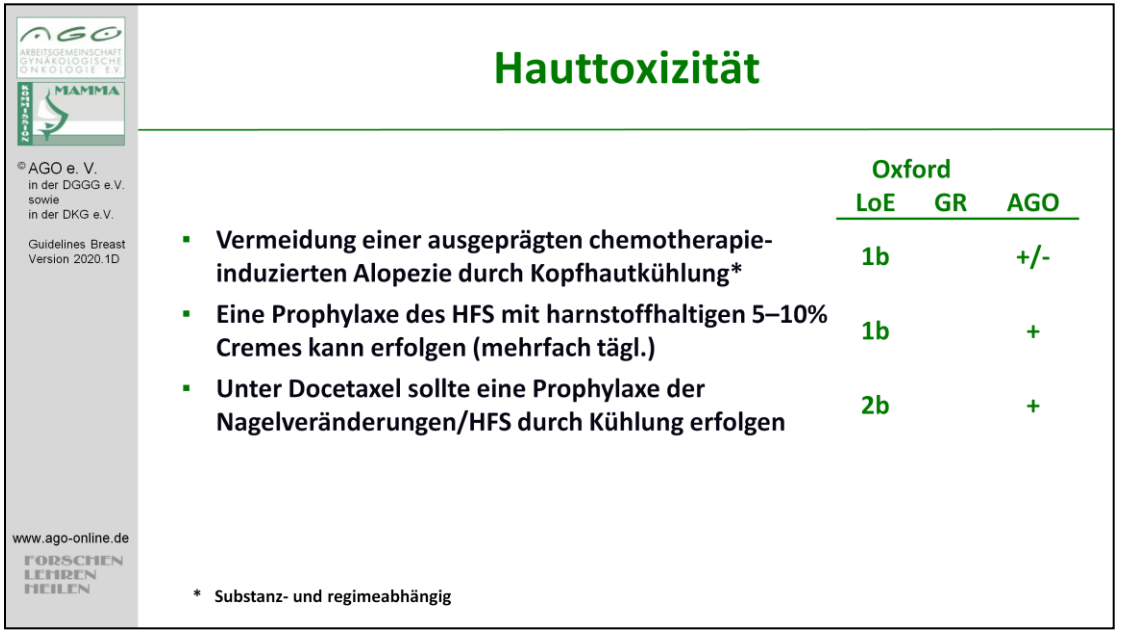

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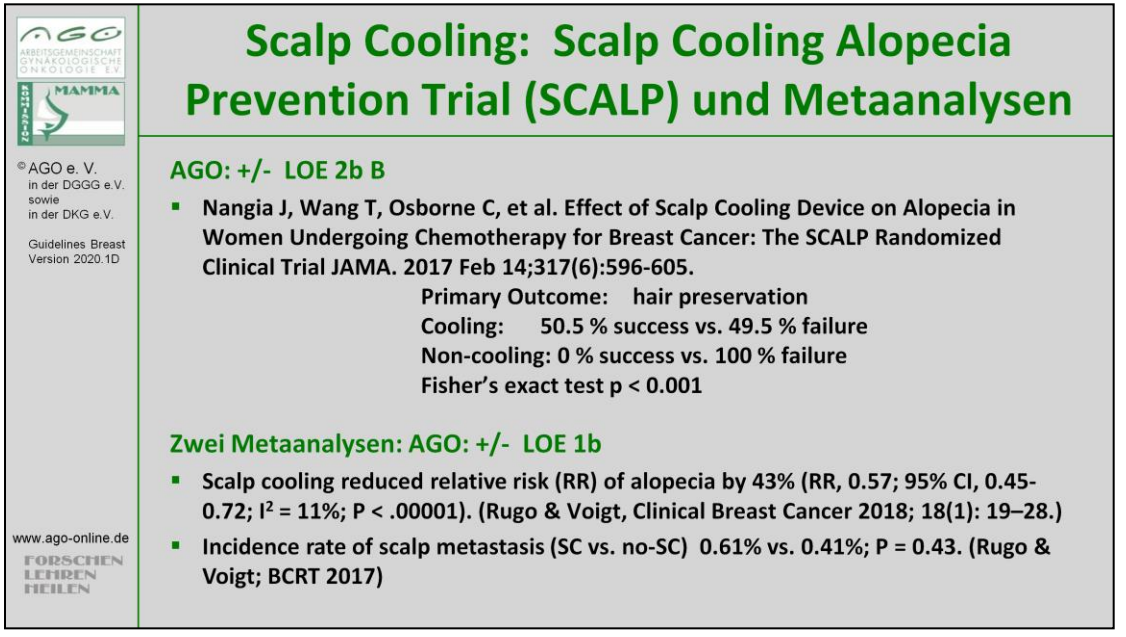
Scalp Cooling:

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.
2. Rugo HS, Voigt J. Scalp Hypothermia for Preventing Alopecia During Chemotherapy. A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Clin Breast Cancer. 2018 Feb;18(1):19-28.
3. Rugo HS, Melin SA, Voigt J. Scalp cooling with adjuvant/neoadjuvant chemotherapy for breast cancer and the risk of scalp metastases: systematic review and meta-analysis. Breast Cancer Res Treat. 2017 Jun;163(2):199-205.



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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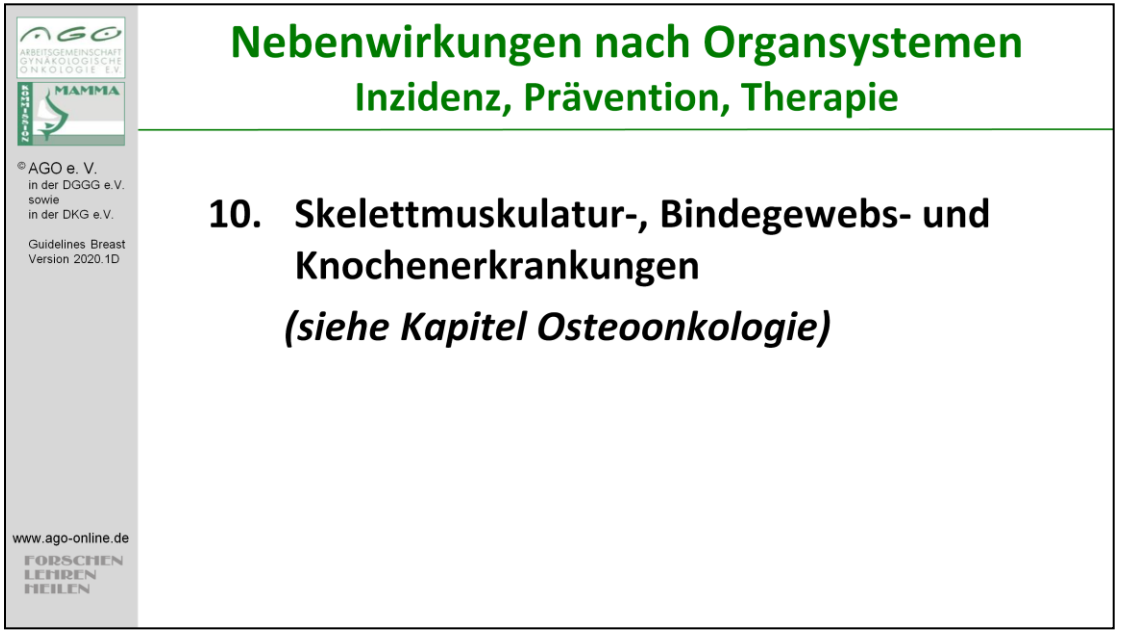

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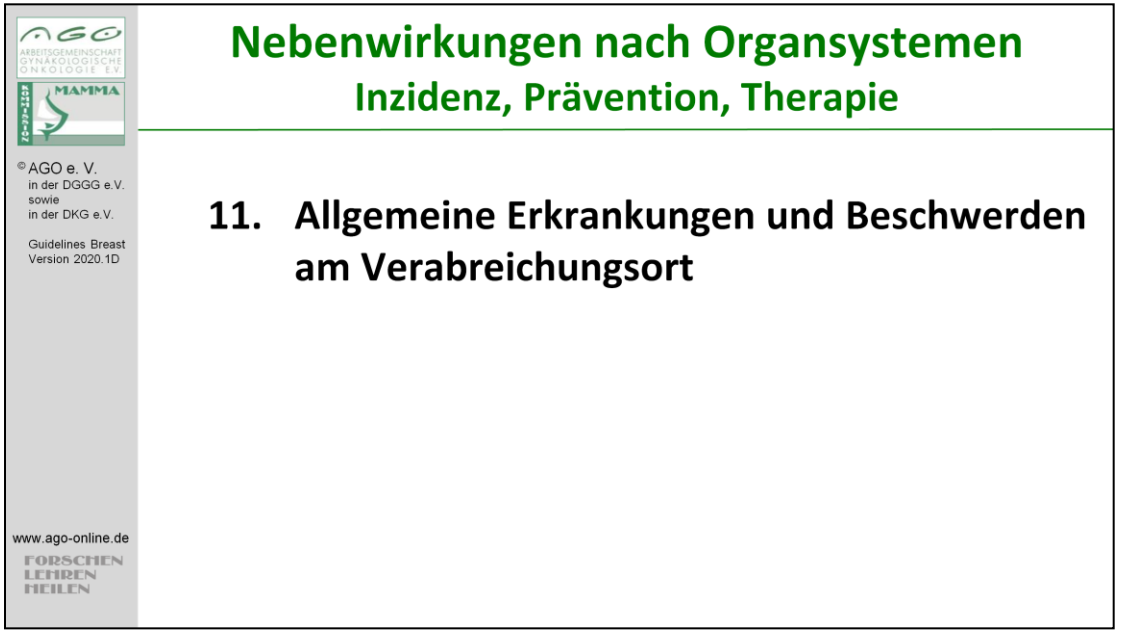

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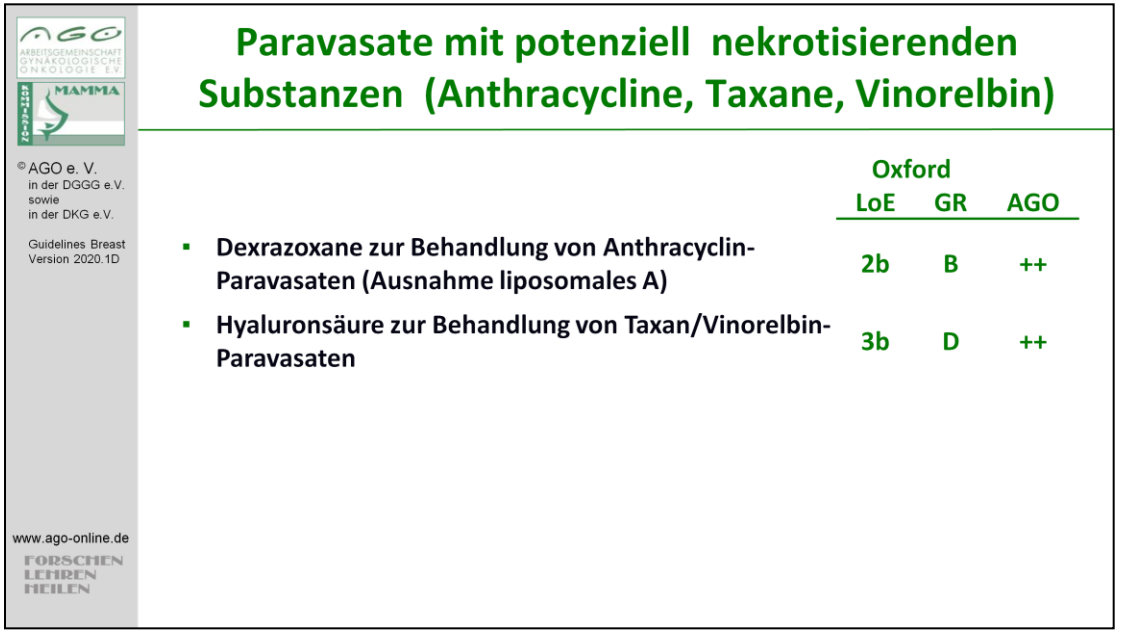

Relevant practice guideline:

1. American Society of Clinical Oncology 2008 clinical practice guideline update: use of chemotherapy and radiation therapy protectants.
2. 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)

Dexrazoxane

1. Hensley ML, Hagerty KL, Kewalramani T, et al.: Cardioprotective effect of dexrazoxane in patients with breast cancer treated with anthracyclines in adjuvant setting: a 10-year single institution experience. J Clin Oncol. 2009 Jan 1;27(1):127-45.
2. Testore F, Milanese S, Ceste M, et al.: Dexrazoxane (Totect): FDA review and approval for the treatment of accidental extravasation following intravenous anthracycline chemotherapy. Oncologist. 2008 Apr;13(4):445-50.
3. Mouridsen HT, Langer SW, Buter J, et al.: Treatment of anthracycline extravasation with Savene (dexrazoxane): results from two prospective clinical multicentre studies. Ann Oncol. 2007 Mar;18(3):546-50.

Hyaluronsäure

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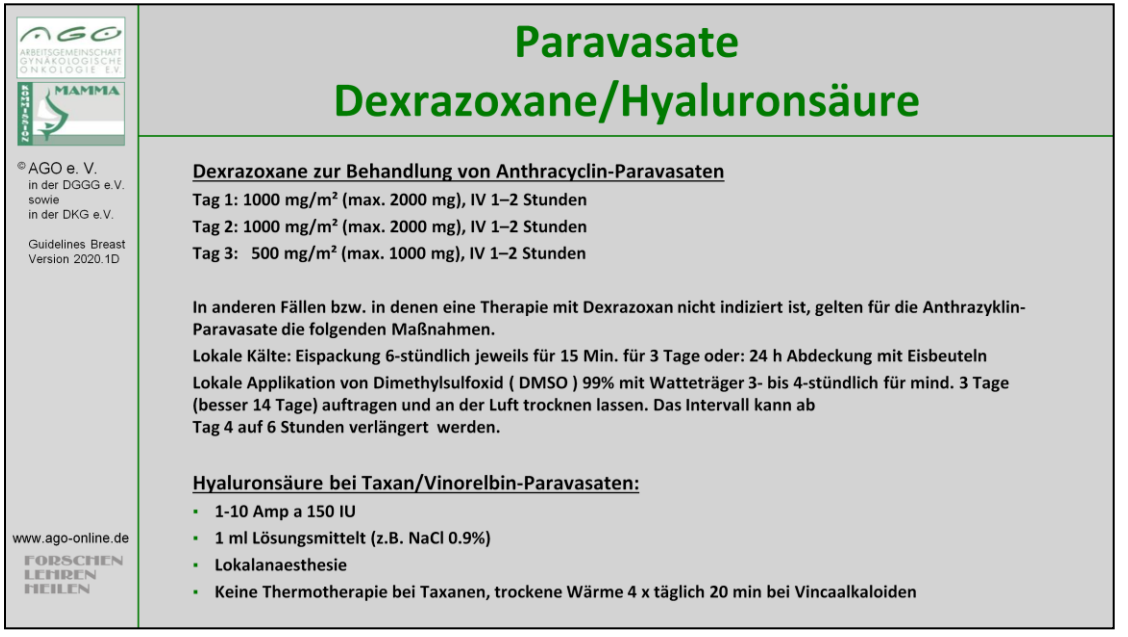

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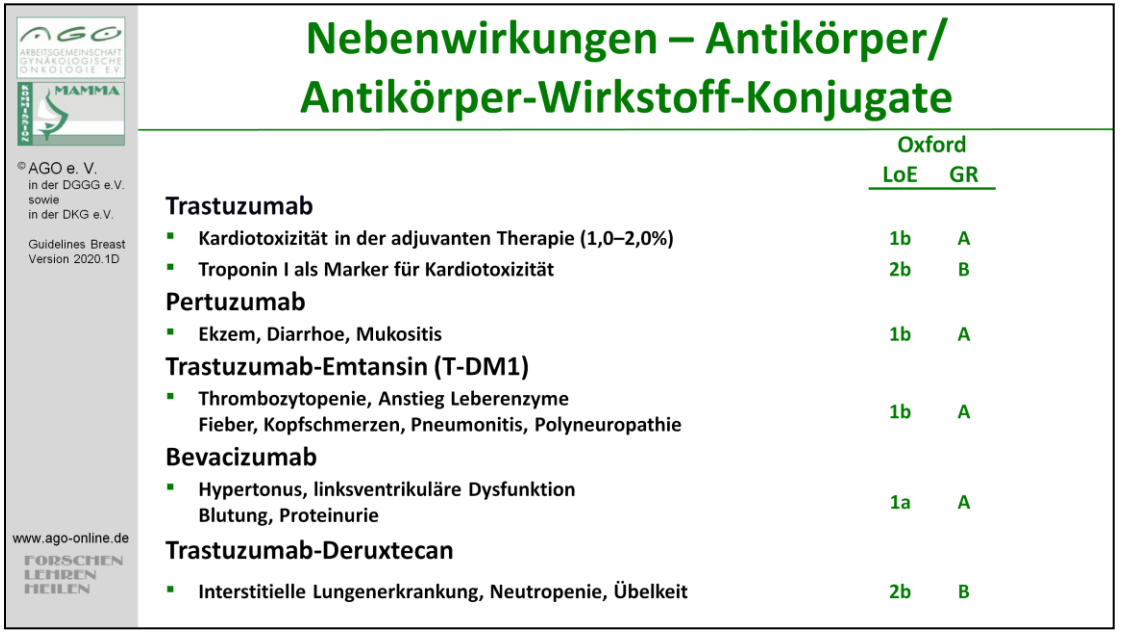
- **Substanzspezifische Nebenwirkungen**
  - **Antikörper und Antikörper-Wirkstoff-Konjugate (ADC)**
  - **CDK 4/6-Inhibitoren**
  - **PARP-Inhibitoren**
  - **Small molecules (TKI, mTOR-Inihibitor)**
  - **Immun-Checkpoint-Antikörper**
  - **PI3-Kinase-Inhibitoren (Alpelisib)**



Cardiotoxicity….

1. Slamon D, Eiermann W, Robert N et al: Adjuvant trastuzumab in HER2-positive breast cancer. N Engl J Med 365:1273-1283, 2011
2. Procter M, Suter TM, de Azambuja, et al: Longer-term assessment of trastuzumab-related cardiac adverse events in the Herceptin Adjuvant (HERA) trial. J Clin Oncol 28: 3422-3428, 2010
3. Russell SD, Blackwell KL, Lawrence J, et al: Independent adjudication of symptomatic heart failure with the use of doxorubicin and cyclophosphamide followed by trastuzumab adjuvant therapy: a combined review of cardiac data from the National Surgical Adjuvant breast and Bowel Project B-31 and the North Central Cancer Treatment Group N9831 clinical trials. J Clin Oncol 28: 3416-3421, 2010
4. Higa GM, Abraham J: Biological mechanisms of bevacizumab-associated adverse events. Expert. Rev Anticancer Ther 2009;9:999–1007
5. Martin M, Esteva FJ, Alba E, et al: Minimizing cardiotoxicity while optimizing treatment efficacy with trastuzumab: review and expert recommendations. Oncologist 2009;14:1–11
6. Untch M, Eidtmann H, du Bois A, et al: Cardiac safety of trastuzumab in combination with epirubicin and cyclophosphamide in women with metastatic breast cancer: results of a phase I trial. Eur J Cancer 2004; 40:988–97
7. Cameron D, Piccart-Gebhart MJ, Gelber RD, et al.: Herceptin Adjuvant (HERA) Trial Study Team. 11 years' follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive early breast cancer: final analysis of the HERceptin Adjuvant (HERA) trial. Lancet.

2017 Mar 25;389(10075):1195-1205.
8. Pondé NF, Lambertini M, de Azambuja E. Twenty years of anti-HER2 therapy-associated cardiotoxicity. ESMO Open. 2016 Jul 21;1(4):e000073.

Troponin I….
1. Cardinale D, Colombo A, Torrisi R, et al: Trastuzumab-induced cardiotoxicity: clinical and prognostic implications of troponin I evaluation. J Clin Oncol 28: 3910-3916, 2010

Bevacizumab ….
1. Cortes J, Calvo V, Ramirez-Merino N et al: Adverse events risk associated with bevacizumab addition to breast cancer chemotherapy: a metanalysis. Ann Oncol. 2019 Jan 9. doi: 10.1093/annonc/mdy535
2. Hamilton EP, Blackwell KL: Safety of Bevacizumab in patients with metastatic breast cancer. Oncology 80:314-325, 2011
3. Syrigos KN, Karapanagiotu E, Boura P et al: Bevacizumab-induced hypertension. Biodrugs; 25:159-169, 2011
4. Blowers E, Hall K: Managing adverse events in the use of bevacizumab and chemotherapy. Br J Nurs 2009;18:351–6, 58
5. Miller K, Wang M, Gralow J, et al: Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. N Engl J Med 357: 2666-2676, 2007

Lapatinib…
1. Wu PA, Balagula Y, Lacouture ME, et al.: Prphylaxs and treatment of dermatologic adverse events from epidermal growth factor receptor inhibitors. Curr Opin Oncol 23:343-351, 2011
2. Von Minckwitz G, Eidtmann H, Loibl S et al:Integrating bevacizumab, everolimus, and lapatinib into current neoadjuvant chemotherapy regimen for primary breast cancer.Safety results of the GeparQuinto trial. Ann Oncol 22:301-306, 2011
3. Sherill B, Amonkar MM, Sherif B et al: Quality of life in hormone receptor-positive Her2-positive metastatic breast cancer patients during treatment with letrozole alone or in combination with lapatinib. Oncologist 15:944-953, 2010
4. Cameron D, Casey M, Olica C et al: Lapatinib plus capecitabine in women with Her2-positive advanced breast cancer: Final survival analysis of a phase III randomized trial. Oncologist 15:924-934, 2010
5. Geyer CE, Forster J, Lindquist D; et al: Lapatinib plus capecitabine for HER2-positive advanced breast cancer. N Engl J Med 355:2733-2743, 2006

Pertuzumab

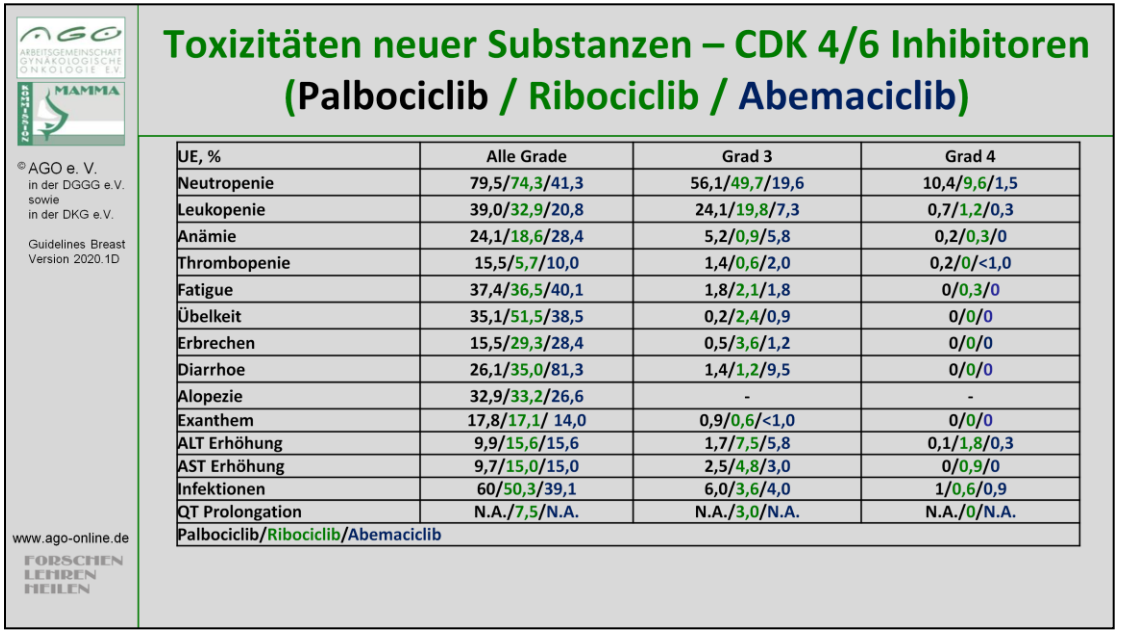
1. von Minckwitz G, Procter M, de Azambuja E, et al. APHINITY Steering Committee and Investigators. Adjuvant Pertuzumab and Trastuzumab in Early HER-2 Positive Breast Cancer. N Engl J Med. 2017 Jul 13;377(2):122-131.
2. Drucker AM, Wu S, Dang CT, et al.: Risk of rash with the anti-HER2 dimerization antibody pertuzumab: a meta-analysis. Breast Cancer Res Treat. 2012 Sep;135(2):347-54.
3. Baselga J, Cortes J, Kim S-B et al. Pertuzumab plus Trastuzumab plus Docetaxel for metastatic breast cancer. N Engl J Med 2012; 366:109-119

T-DM1

1. Verma S, Miles D, Gianni L, et al: EMILIA Study Group. Trastuzumab emtansine for HER2-positive advanced breast cancer. N Engl J Med. 2012 Nov 8;367(19):1783-91.
2. von Minckwitz G, Huang CS, Mano MS, et al.; KATHERINE Investigators. Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer. N Engl J Med. 2018 Dec 5. doi: 10.1056/NEJMoa1814017

Trastuzumab-Deruxtecan

1. Modi S, Saura C, Yamashita T, et al.: Trastuzumab deruxtecan in previously treated her2-positive breast cancer. N Engl J Med 2019.
2. Tamura K, Tsurutani J, Takahashi S, et al.: Trastuzumab deruxtecan (ds-8201a) in patients with advanced her2-positive breast cancer previously treated with trastuzumab emtansine: A dose-expansion, phase 1 study. Lancet Oncol 2019;20:816-826.



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

Palbociclib

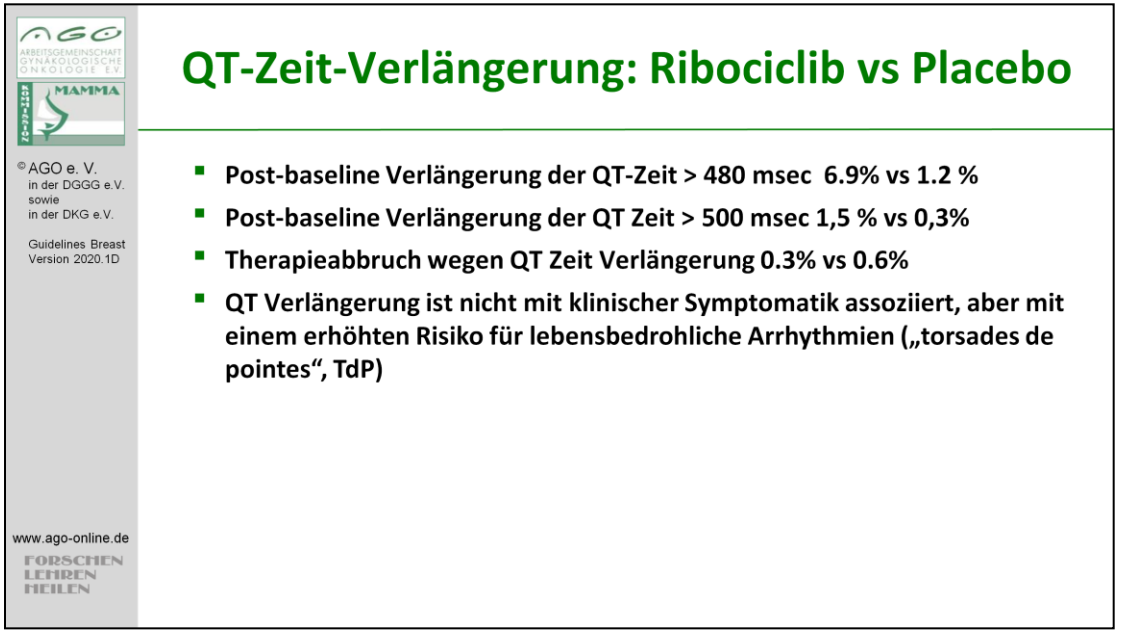
1. Verma S, Bartlett CH, Schnell P, et al. Palbociclib in Combination With Fulvestrant in Women With Hormone Receptor-Positive/HER2-Negative Advanced Metastatic Breast Cancer: Detailed Safety Analysis From a Multicenter, Randomized, Placebo-Controlled, Phase III Study (PALOMA-3). Oncologist. 2016 Oct;21(10):1165-1175. Epub 2016 Jul 1.
2. N.Harbeck, J. Ettl, Palbociclib, CDK 4/ 6 Inhibition als neue Therapieoption bei Patientinnen mit fortgeschrittenem HR+/ Her – Mammakarzinom. Drug Report, 2017

Ribociclib

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.



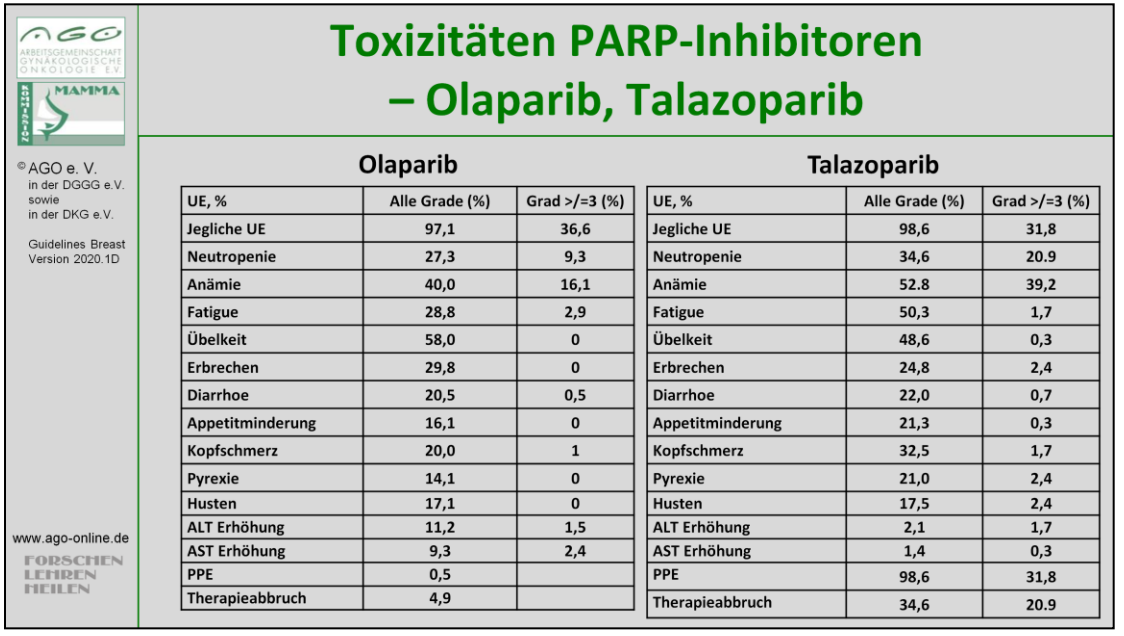
1. Tripathy D, Im SA, Colleoni M, et al. Ribociclib plus endocrine therapy for premenopausal women with hormone-receptor-positive, advanced breast cancer (MONALEESA-7): a randomized phase 3 trial. Lancet Oncol. 2018 Jul;19(7):904-915.
2. Slamon DJ, Neven P, Chia S, et al. Phase III Randomized Study of Ribociclib and Fulvestrant in Hormone-Receptor-Positive, Human Epidermal Growth Factor Receptor-2 Negative Advanced Breats Cancer: MONALEESA-3. J Clin Oncol. 2018 Aug 20;36(24):2465-2472.
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.

Toxizitäten neuer Substanzen: mTOR-Inhibitor (Everolimus)

Guidelines Breast
Version 2020.1D

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

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



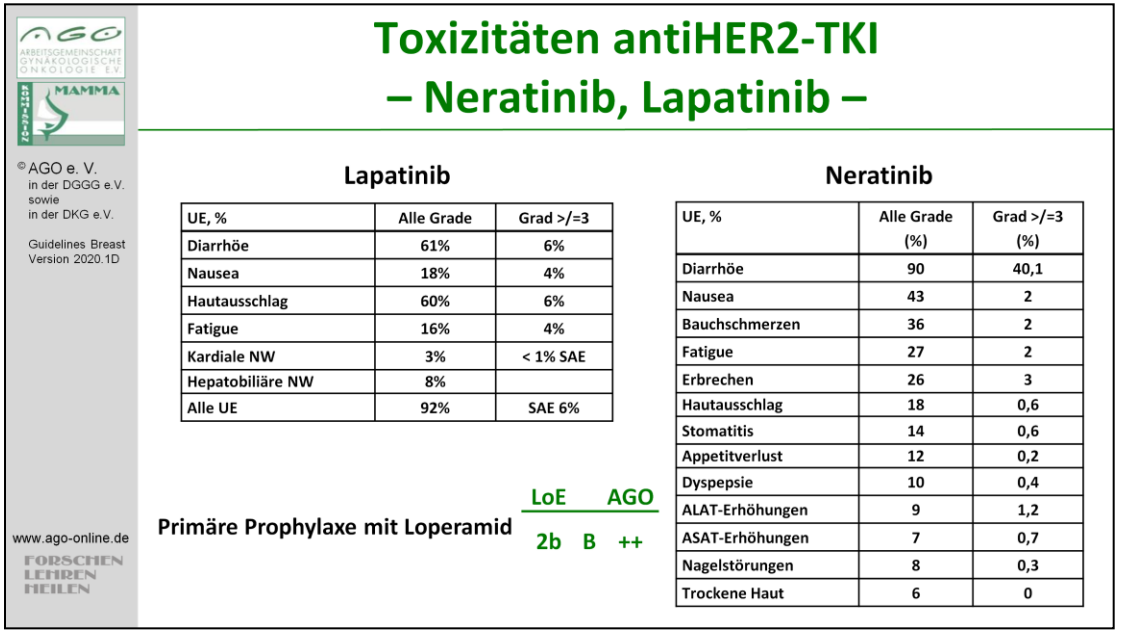
Olaparib

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

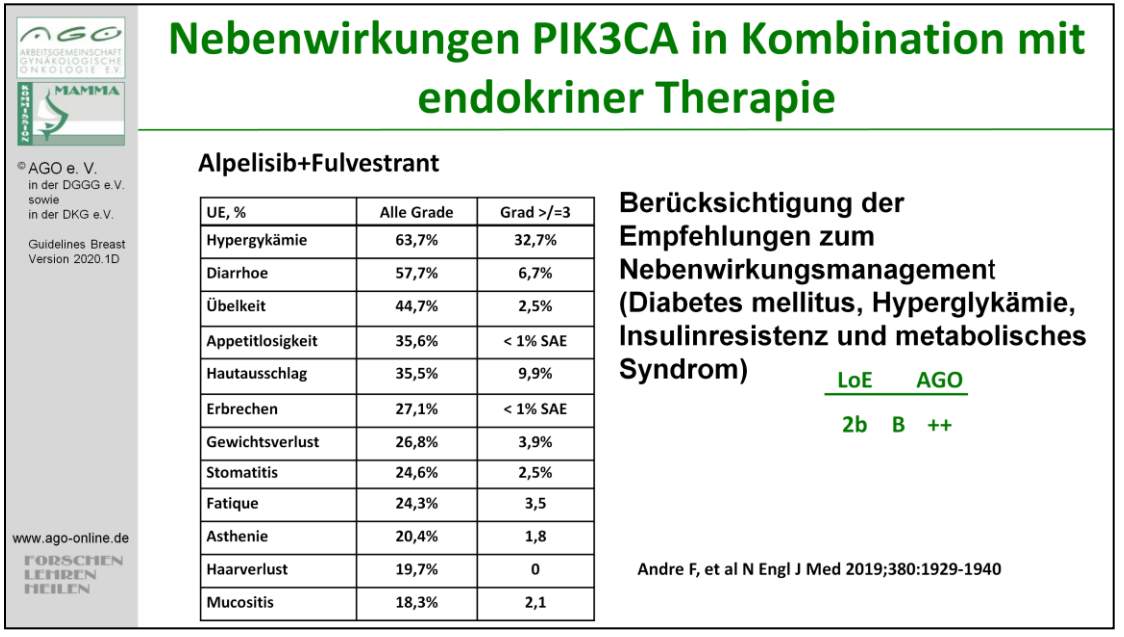
Talazoparib

UE, %	Alle Grade (%)	Grad >/=3 (%)
Jegliche UE	98,6	31,8
Neutropenie	34,6	20.9
Anämie	52.8	39,2
Fatigue	50,3	1,7
Übelkeit	48,6	0,3
Erbrechen	24,8	2,4
Diarrhoe	22,0	0,7
Appetitminderung	21,3	0,3
Kopfschmerz	32,5	1,7
Pyrexie	21,0	2,4
Husten	17,5	2,4
ALT Erhöhung	2,1	1,7
AST Erhöhung	1,4	0,3
PPE	98,6	31,8
Therapieabbruch	34,6	20.9

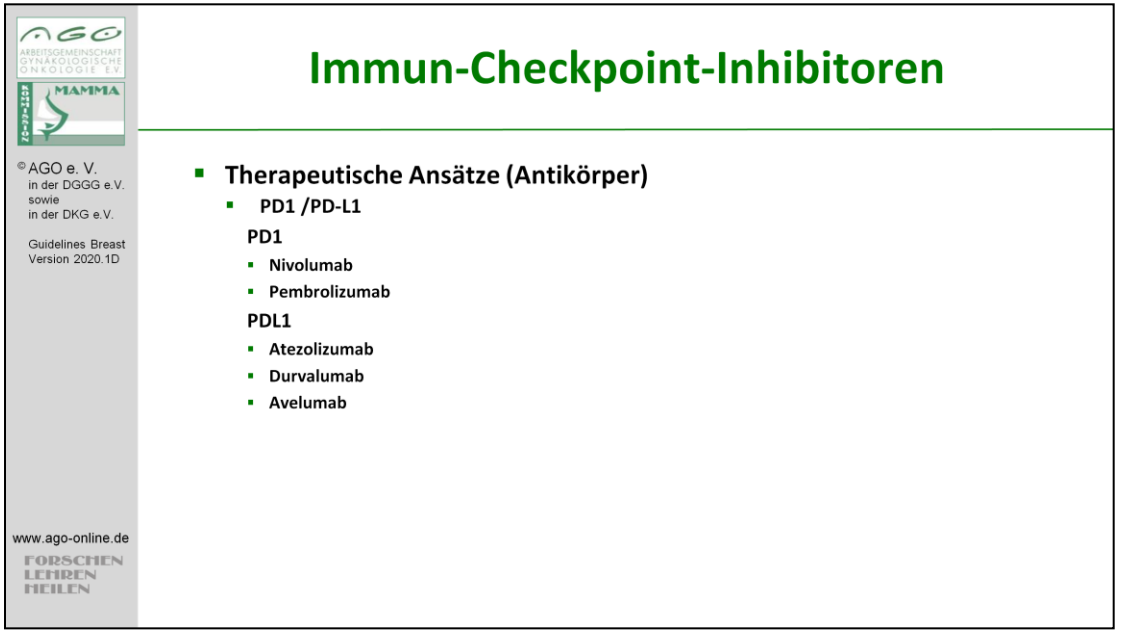
1. Litton JK, Rugo HS, Ettl J, et al. Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation. N Engl J Med. 2018 Aug 23;379(8):753-763.
2. Robson M, Im SA, Senkus E et al. Olaparib for metastatic breast cancer in patients with germline BRCA mutation N Engl J Med 377: 523-533, 2017



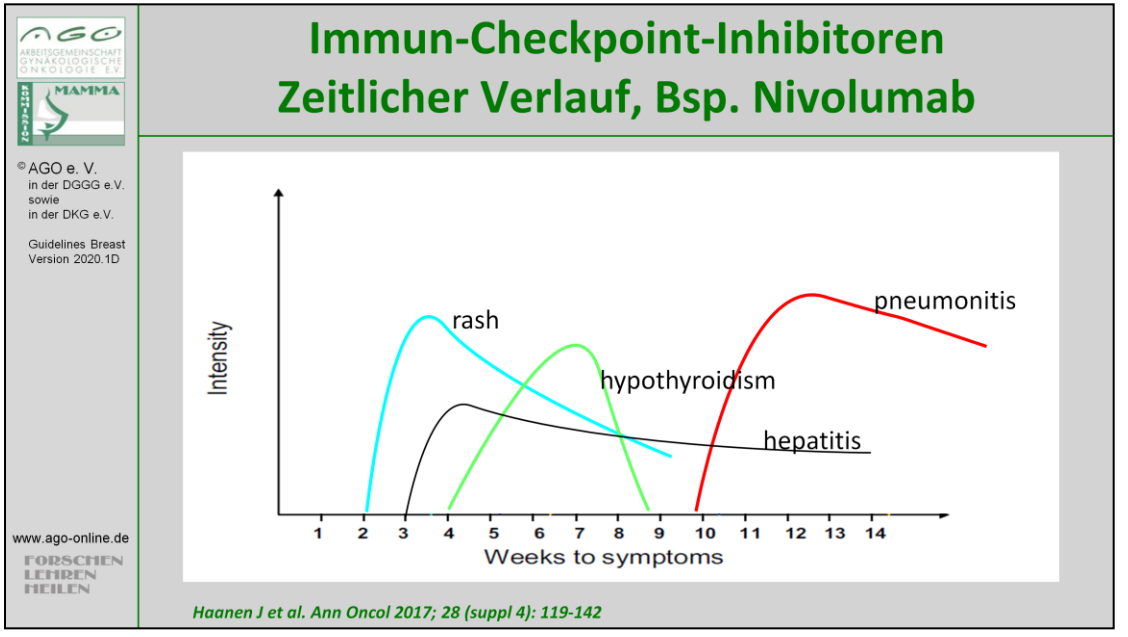
1. Chan A, Delagoge S, Holmes FA et al Neratinib after trastuzumab –based adjuvant therapy in patients with HER2 positive breast cancer (ExteNET): a multicentr, randomized, double.-blind, placebo controlled , phase III trial. Lancet Oncol 17(39: 367-377, 2016
2. Piccart-Gebhart M , Holmes E., Baselga J et al Adjuvant Lapatinib and Trastuzumab for Early Human Epidermal Growth Factor Receptor 2-positive Breast Cancer:Results From the Randomized Phase III Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization Trial. JCO 34:1034-1042, 2015
3. Neratinib: FDA Produktinformation 2017



1. H. S. Rugo, F. André, et al. Time Course and Management of Key Adverse Events During the Randomized Phase 3 SOLAR-1 Study of PI3K inhibitor Alpelisib Plus Fulvestrant in Patients With HR-Positive Advanced Breast Cancer in press, 2020
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.
3. Mayer IA, Abramson V, Formisano L, et al.: A phase ib study of alpelisib (byl719), a pi3kalpha-specific inhibitor, with letrozole in er+/her2-negative metastatic breast cancer. Clin Cancer Res 2016.



1. Haanen J, Carbonnel F, Robert C, et al, on behalf of the ESMO Guidelines Committee: Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelöines for diagnosis, treatment and follow-up. Ann Oncol 2017; 28 (suppl 4): 119-142. doi: ^0.1093/annonc/mdx225
2. Ingrid A. Mayer1, Aleix Prat2, Daniel Egle3, et al.: A Phase II Randomized Study of Neoadjuvant Letrozole Plus Alpelisib for Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative Breast Cancer (NEO-ORB) Clin Cancer Res. 2019 May 15; 25(10): 2975–2987.



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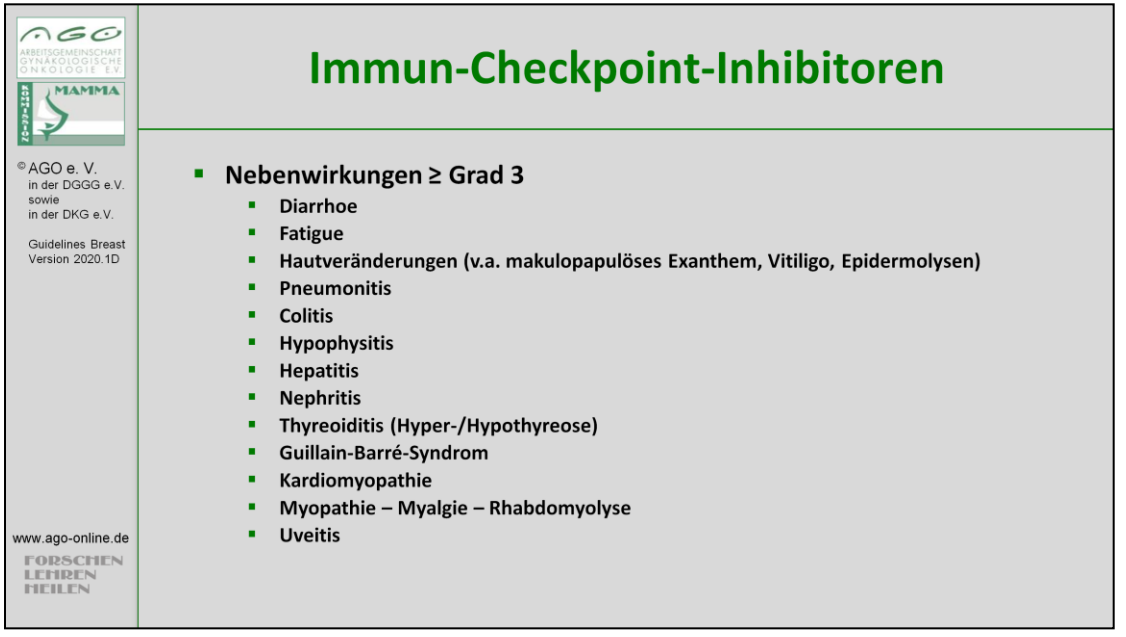

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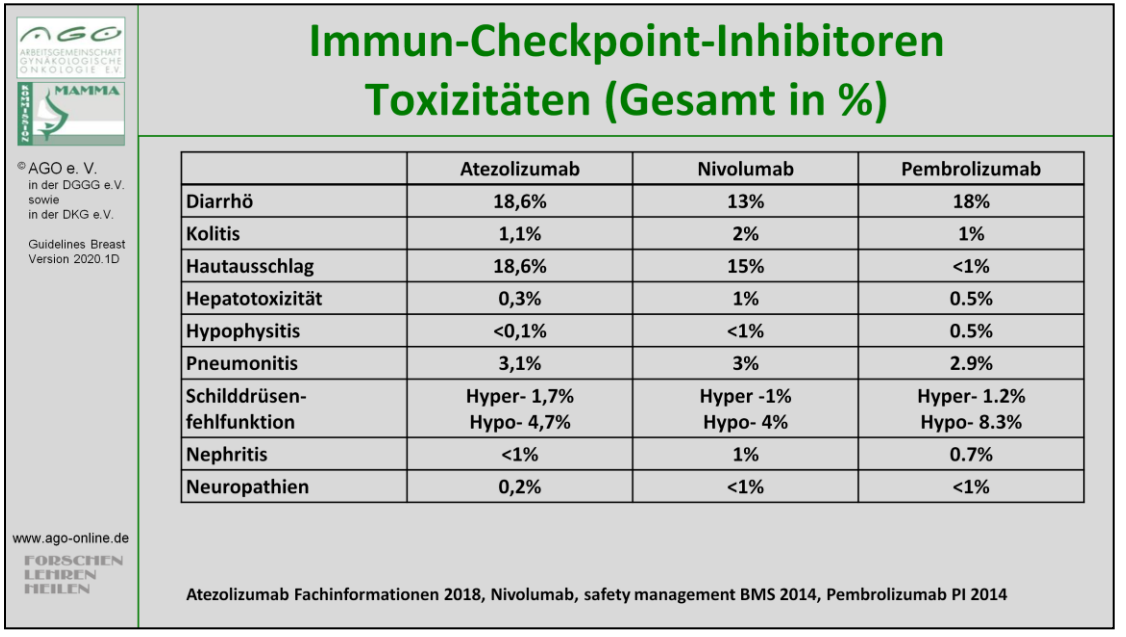
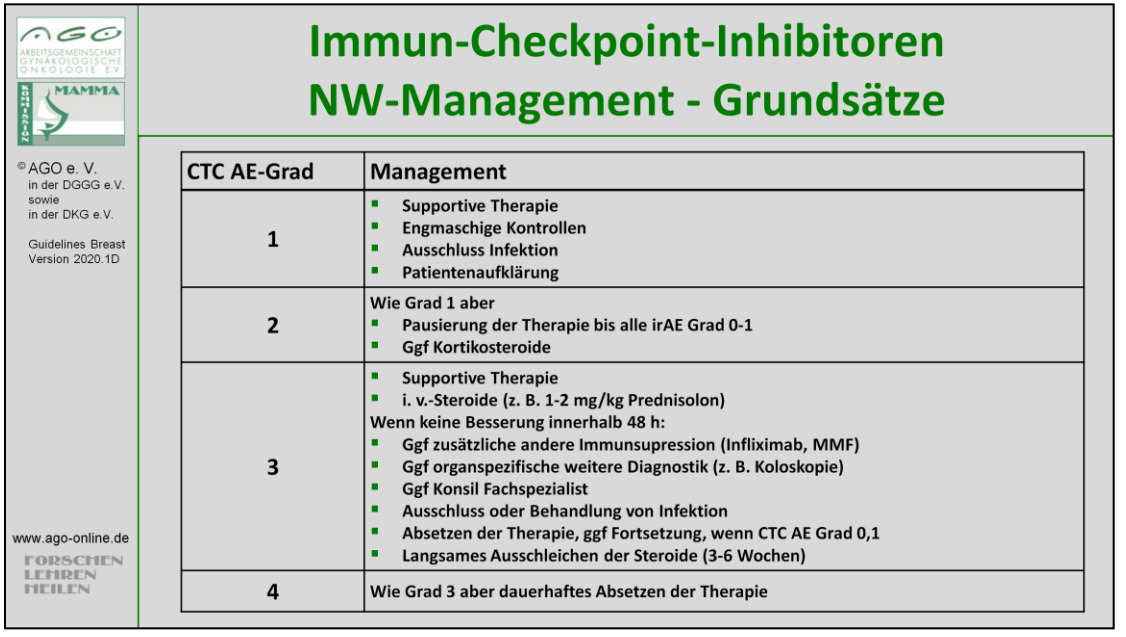


Immun-Checkpoint-Inhibitoren
Toxizitäten (Gesamt in %)

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

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

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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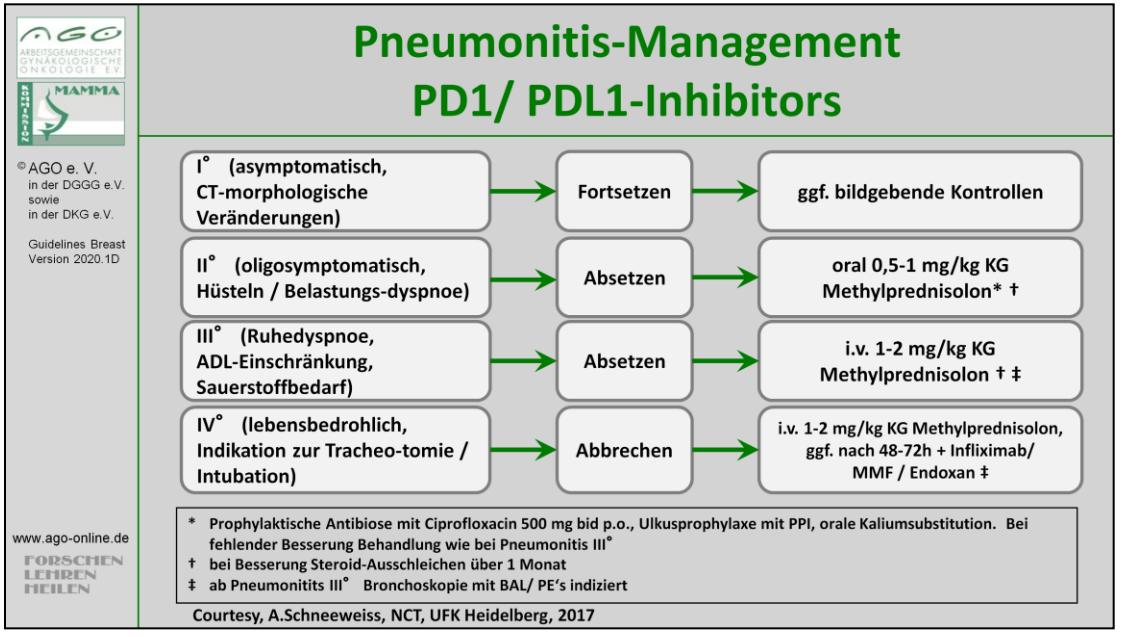
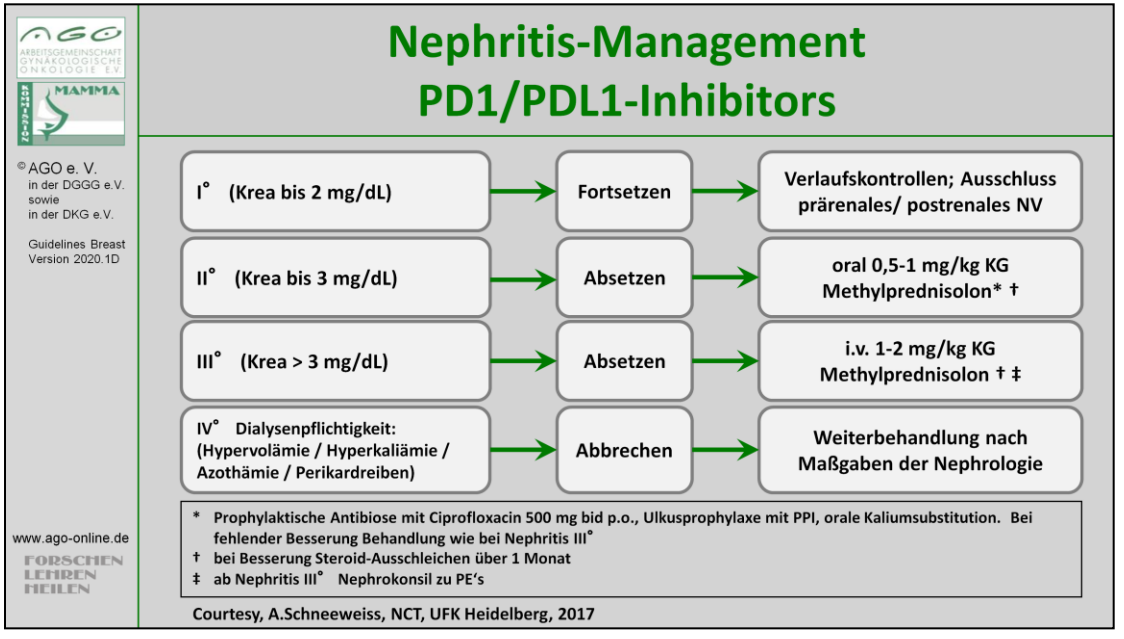


1. Haanen J, Carbonnel F, Robert C, et al. on behalf of the ESMO Guidelines Committee: Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017; 28 (suppl 4): 119-142.
2. Postow M, Sidlow R, Hellmann M: Immune-related adverse events associated with immune checkpoint blockade. N Engl J Med 2018; 378(2): 158-168. doi: 10.1056/NEJMra1703481



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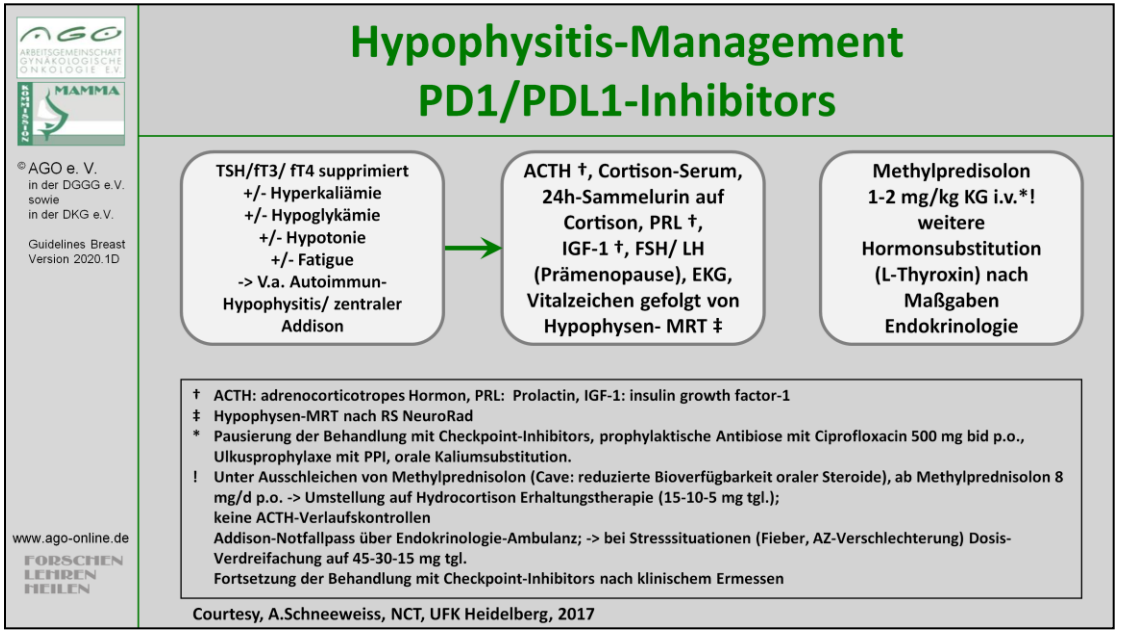

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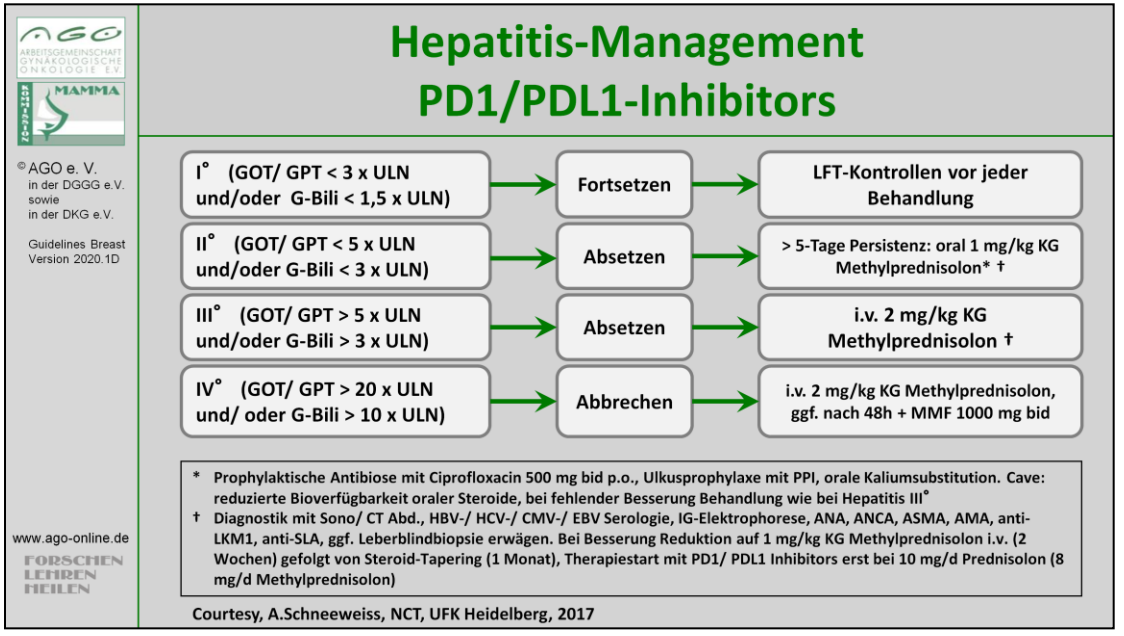

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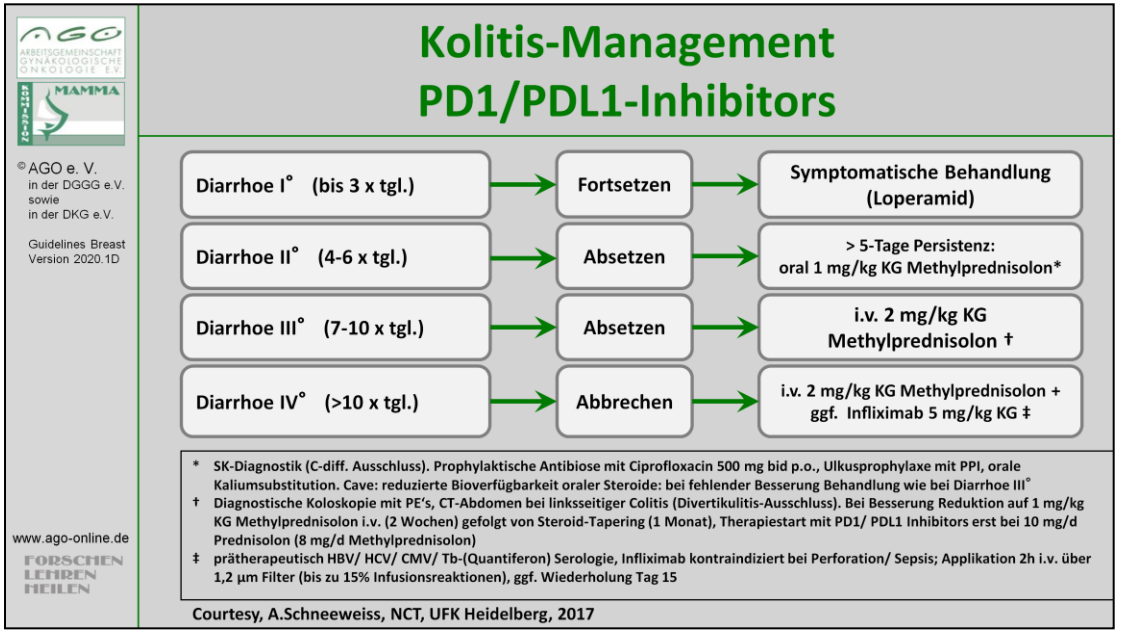

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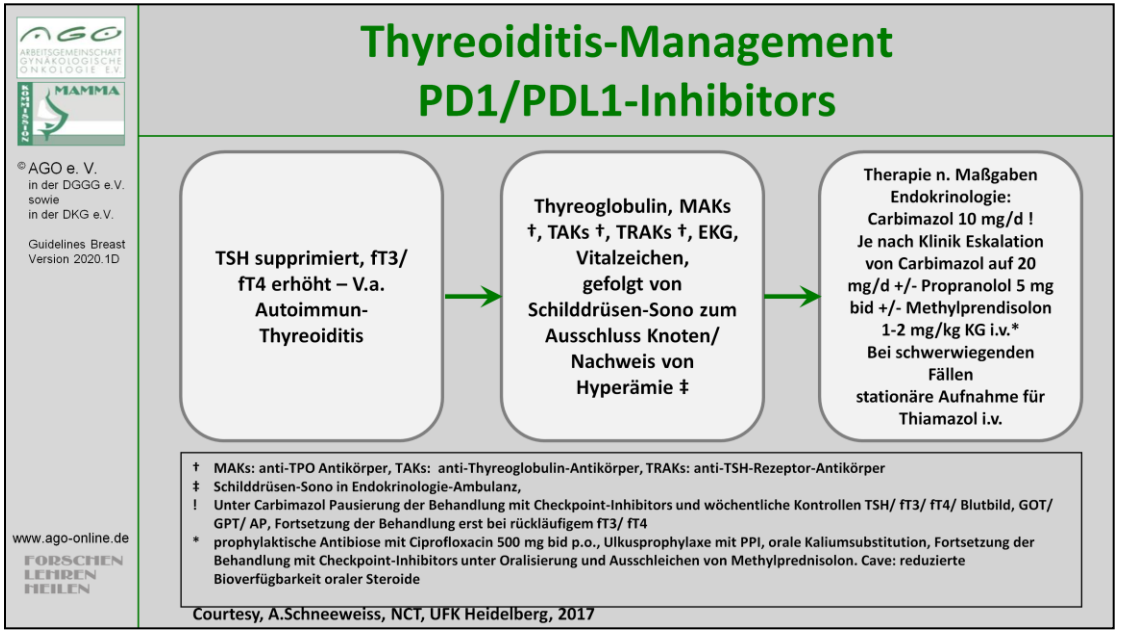
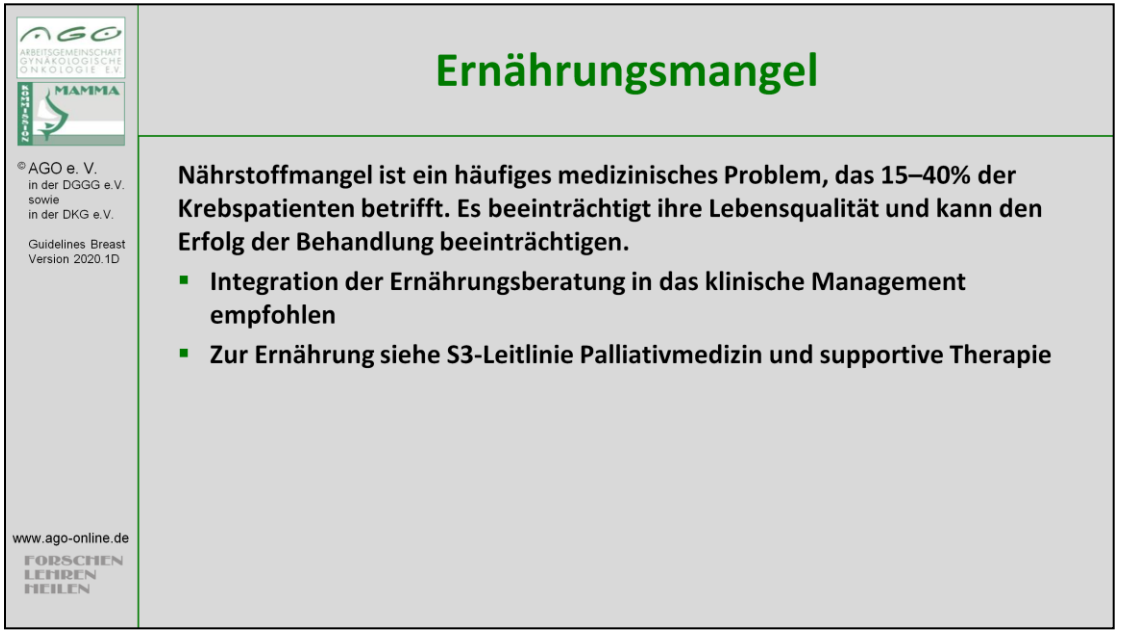


1. Haanen J, Carbonnel F, Robert C, et al. on behalf of the ESMO Guidelines Committee: Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017; 28 (suppl 4): 119-142.
2. Postow M, Sidlow R, Hellmann M: Immune-related adverse events associated with immune checkpoint blockade. N Engl J Med 2018; 378(2): 158-168. doi: 10.1056/NEJMra1703481

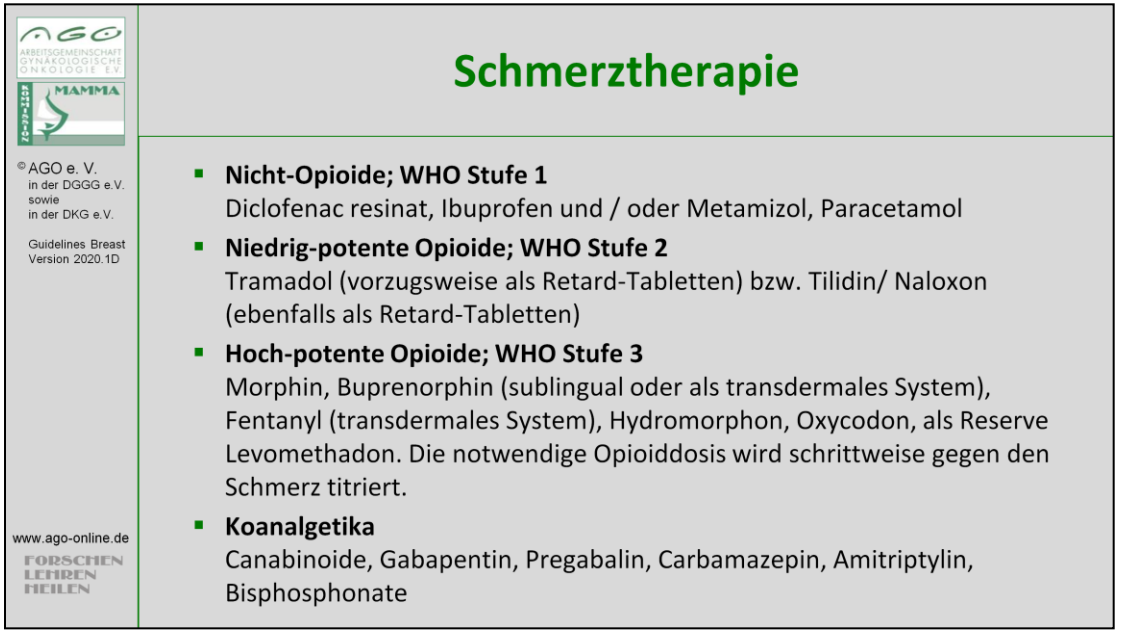
Guidelines Breast
Version 2020.1D

- **Andere supportive und palliative Fragestellungen**
  - **Ernährung**
  - **Schmerztherapie**
  - **Palliative Care**



Klinische Ernährung:

1. Arends J, Bertz H, Bischoff SC, et al. und das DGEM Steering Committee. Klinische Ernährung in der Onkologie. S3-Leitlinie AWMF Reg.: 073-0061Aktuel Ernahrungsmed 2015; 40: e1–e74 www.awmf.org/uploads/tx_szleitlinien/073-006l_S3_Klin_Ernährung_in_der_Onkologie_2015-10.pdf abgerufen 2101202
2. de Las Peñas R, Majem M, Perez-Altozano J, et al SEOM clinical guidelines on nutrition in cancer patients (2018). Clin Transl Oncol. 2019 Jan;21(1):87-93. doi: 10.1007/s12094-018-02009-3. Epub 2019 Jan 8.
3. van den Berg MMGA[1], Kok DE[2], Posthuma L[1], et al Breast Cancer Res Treat. 2019 Jan;173(2):475-481. doi: 10.1007/s10549-018-5014-5. Epub 2018 Oct 23.

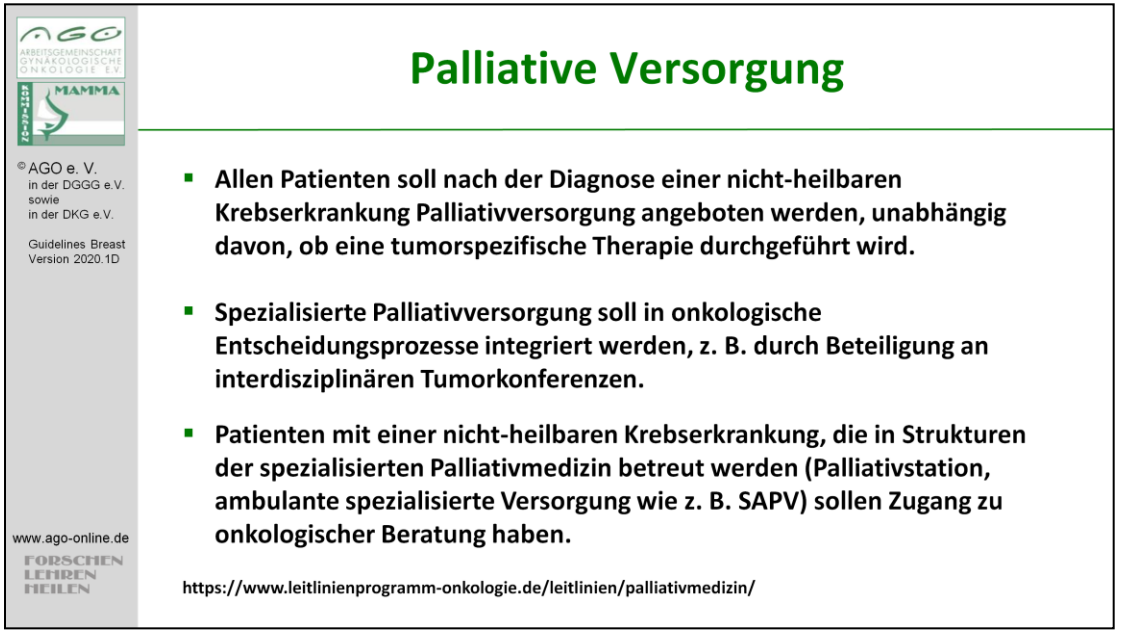


Relevant practice guideline:

1. WHO Guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents. Januar 2019 , Geneva ISBN: 978-92-4-155039-0 www.who.int/ncds/management/palliative-care/cancer-pain-guidelines/en/ Zugriff 21.01.2020

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



1. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Palliativmedizin für Patienten mit einer nicht-heilbaren Krebserkrankung, Lang- version 2.0, 2019, AWMF-Registernummer: 128/001OL, https://www.leitlinienprogramm-onkologie.de/leitlinien/palliativmedizin/ (abgerufen am: 21.01.2020)