# Diagnosis and Treatment of Patients with early and advanced Breast Cancer



Guidelines Breast
Version 2024.1E

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## Supportive Care and Management of Side Effects

Screened data bases

Pubmed 2007 - 2023, ASCO 2010 – 2023, SABCS 2010 – 2023, Cochrane Data Base (2023)

Screened guidelines

1. Cardoso F, Paluch-Shimon S, Senkus E, et. al. 5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5). Ann Oncol. 2020 Dec;31(12):1623-1649.
2. Thomssen C., Lüftner D, Untch M, et al. International Consensus Conference for Advanced Breast Cancer, Lisbon 2019: ABC5 Consensus - Assessment by a German Group of Experts. Breast Care (Basel). 2020
3. ASCO (American Association of Clinical Oncology, Practice Guidelines, 2021) 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 , 2021): http://www.nccn.org
8. S3-Leitlinie: Supportive Therapie: Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3 – Februar 2020 AWMF-Registernummer: 032/054OL

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# Supportive Care and Management of Side Effects

- **Versions 2002–2023:**
  **Albert / Bauerfeind / Brunnert / Bischoff / Costa / Dall / Diel / Fersis / Friedrich / Friedrichs / Gerber / Göhring / Hanf / Harbeck / Heinrich / Huober / Jackisch / Lisboa / Lück / Lüftner / Maass / von Minckwitz / Möbus / Müller / Mundhenke / Nitz / Oberhoff / Park-Simon / Reimer/ Rody / Schaller / Scharl / Schmidt / Schneeweiss / Schütz / Solomayer / Souchon / Stickeler / Thomssen / Untch**
- **Version 2024:**
  **Kolberg-Liedtke / Würstlein**

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# Guidelines – Evidence

**Specific national and international guidelines deal with various aspects of evidence-based supportive therapy of cancer patients.**

**Without claiming completeness, such guidelines will be quoted, with an emphasis on German guidelines.**

**Aspects concerning breast cancer patients will especially be highlighted.**

**The „Arbeitsgemeinschaft Supportive Maßnahmen in der Onkologie, Rehabilitation und Sozialmedizin der DKG“ should especially be highlighted (http://www.onkosupport.de).**

**Multidisciplinary S 3 guidelines of the AWMF (Reg.-Nr. 032-054OL):**

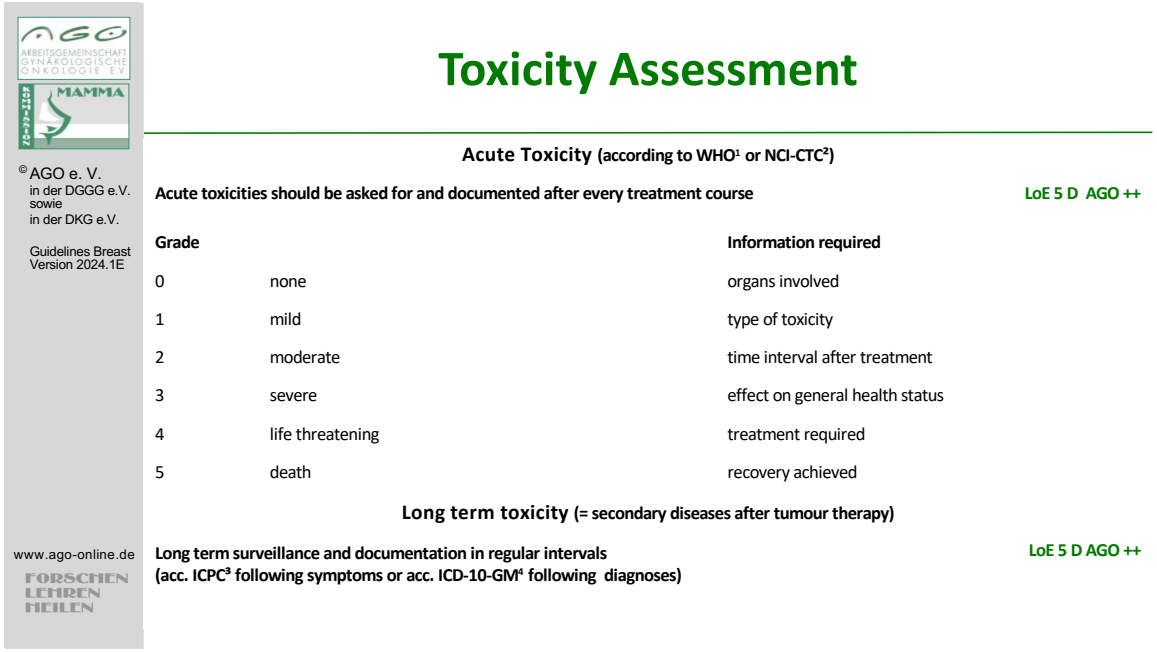
- **S3-Leitlinie: Supportive Therapie bei onkologischen Patientinnen Langversion 1.3 –Februar 2020 AWMF-Registernummer: 032/054OL**

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

2. ESMO Clinical Practice Guidelines: Supportive and Palliative Care. www.esmo.org

3. Jordan K, Aapro M, Kaasa S, et al. European Society for Medical Oncology (ESMO) position paper on supportive and palliative care. Ann Oncol. 2018 Jan 1;29(1):36-43.

4. Schneider BJ, Naidoo J, Santomasso BD, et al. Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update. J Clin Oncol. 2021 Dec 20;39(36):4073-4126.




## Toxicity Assessment

**Acute Toxicity** (according to WHO[1] or NCI-CTC[2])

**Acute toxicities should be asked for and documented after every treatment course** LoE 5 D AGO ++

| Grade | | Information required |
|---|---|---|
| 0 | none | organs involved |
| 1 | mild | type of toxicity |
| 2 | moderate | time interval after treatment |
| 3 | severe | effect on general health status |
| 4 | life threatening | treatment required |
| 5 | death | recovery achieved |

**Long term toxicity** (= secondary diseases after tumour therapy)

**Long term surveillance and documentation in regular intervals** LoE 5 D AGO ++
**(acc. ICPC[3] following symptoms or acc. ICD-10-GM[4] following diagnoses)**


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)

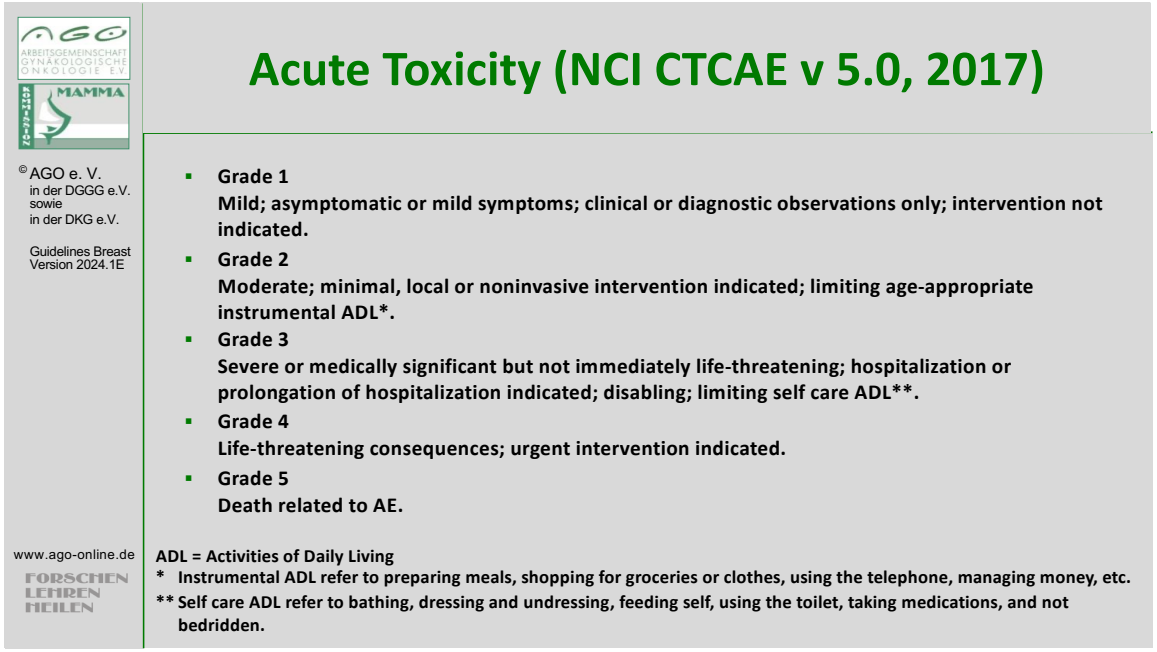
Akute Toxizität nach jedem Therapiezyklus abfragen

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)

# Use of eHealth (DiGA)

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| **Use of DiGA to improve quality of life during and after breast cancer therapy** | 2b | B | +/- |
| **Use of PROs for improved collection of therapy-associated side effects and quality of life** | 2b | B | +/- |

*** See current DiGA status / reimbursement**

DiGAs aktuell: diga.bfarm.de

1. Groene N and Schneck L (2023) Covering digital health applications in the public insurance system: how to foster innovation in patient care while mitigating financial risks— evidence from Germany. Front. Digit. Health 5:1217479. doi: 10.3389/fdgth.2023.1217479
2. Kramer U, Borges U, Fischer F, Hoffmann W, Pobiruchin M, Vollmar HC. DNVF-Memorandum – Gesundheits- und Medizin-Apps (GuMAs). Das Gesundheitswesen 2019; 81(10): 154 - 170. DOI: 10.1055/s-0038-1667451
3. Vollmar HC, Kramer U, Müller H, Griemmert M, Noelle G, Schrappe M. Position Paper of The AG Digital Health DNVF on Digital Health Applications: Framework Conditions For Use in Health Care, Structural Development and Science. Gesundheitswesen. 2017 Dec;79(12):1080-1092. doi: 10.1055/s-0043-122233. Epub 2017 Dec 29.; 12/2017
4. Wanchai, A, Anderson EA, and Armer JM. "A Systematic Review of M-Health Apps on Managing Side Effects of Breast Cancer Treatment." [In eng]. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 31, no. 1 (2022-12-27 2022): 86. https://doi.org/doi:10.1007/s00520-022-07464-x. https://pubmed.ncbi.nlm.nih.gov/36574048/
5. Horn A, Jírů-Hillmann S, Widmann J, Montellano FA, Salmen J, Pryss R, Wöckel A, Heuschmann PU. Systematic review on the effectiveness of mobile health applications on mental health of breast cancer survivors. Journal of Cancer Survivorship https://doi.org/10.1007/s11764-023-01470-6

6. Singleton AC, Raeside R, Hyun KK, Partridge SR, Di Tanna GL, Hafiz N, Tu Q, et al. "Electronic Health Interventions for Patients with Breast Cancer: Systematic Review and Meta-Analyses." [In eng]. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 40, no. 20 (2022-7-10 2022): 2257-70. https://doi.org/doi:10.1200/JCO.21.01171. https://pubmed.ncbi.nlm.nih.gov/35500200/.
7. Cruz FOAM,, Vilela RA, Ferreira EB, Melo NS, and Reis PEDD. "Evidence on the Use of Mobile Apps During the Treatment of Breast Cancer: Systematic Review." [In eng]. JMIR mHealth and uHealth 7, no. 8 (2019-8-27 2019): e13245. https://doi.org/doi:. https://pubmed.ncbi.nlm.nih.gov/31456578/.
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9. Jongerius C, Russo S, Mazzocco K, and Pravettoni G. "Research-Tested Mobile Apps for Breast Cancer Care: Systematic Review." [In eng]. JMIR mHealth and uHealth 7, no. 2(2019-2-11 2019): e10930. https://doi.org/doi:. https://pubmed.ncbi.nlm.nih.gov/30741644/
10. Uncovska M, Freitag B, Meister S, Fehring L Rating analysis and BERTopic modeling of consumer versus regulated mHealth app reviews in Germany. Digital Medicine (2023)6:115 ; https://doi.org/10.1038/s41746-023-00862-3
11. Uncovska M, Freitag B, Meister S, Fehring L Rating Patient Acceptance of Prescribed and Fully Reimbursed mHealth Apps in Germany: An UTAUT2-based Online Survey Study.Journal of Medical Systems (2023) 47:14 https://doi.org/10.1007/s10916-023-01910-x
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15. Harbeck N, Kates R, Schinköthe T, Schumacher J, Wuerstlein R, Degenhardt T, Lüftner D, Räth P, Hoffmann O, Lorenz R, Decker T, Reinisch M, Göhler T, Staib P, Gluz O, Fasching PA, Schmidt M; AGO-B, WSG PreCycle investigators. Favorable impact of therapy

management by an interactive eHealth system on severe adverse events in patients with hormone receptor-positive, HER2-negative locally advanced or metastatic breast cancer treated by palbociclib and endocrine therapy. Cancer Treat Rev. 2023 Dec;121:102631. doi: 10.1016/j.ctrv.2023.102631. Epub 2023 Oct 18. PMID: 37862832

# Chemotherapy – Acute Toxicities I



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

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

Side effect categories - MedDRA (Medical Dictionary for Regulatory Activities)

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

Sources for product information (Download 19.01.2018)

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

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

Further references (selection)


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2. Petrelli F et al: Mortality, leukemic risk, and cardiovascular toxicity of adjuvant anthracycline and taxane chemotherapy in breast cancer: a meta-analysis. Breast Cancer Res Treat. 2012 Sep;135(2):335-46
3. Jim HS et al: Meta-analysis of cognitive functioning in breast cancer survivors previously treated with standard-dose chemotherapy. J Clin Oncol. 2012 Oct 10;30(29):3578-87
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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.
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9. Basch E, Prestrud AA, Hesketh PJ, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. Journal of Clinical Oncology 2011;29:4189- 4198
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.

# Chemotherapy – Acute Toxicities II



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

- unknown (based on available data incidence not assessable)

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

Abbreviations

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

Side effect categories - MedDRA (Medical Dictionary for Regulatory Activities)

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

Sources for product information (Download 19.01.2018)

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

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

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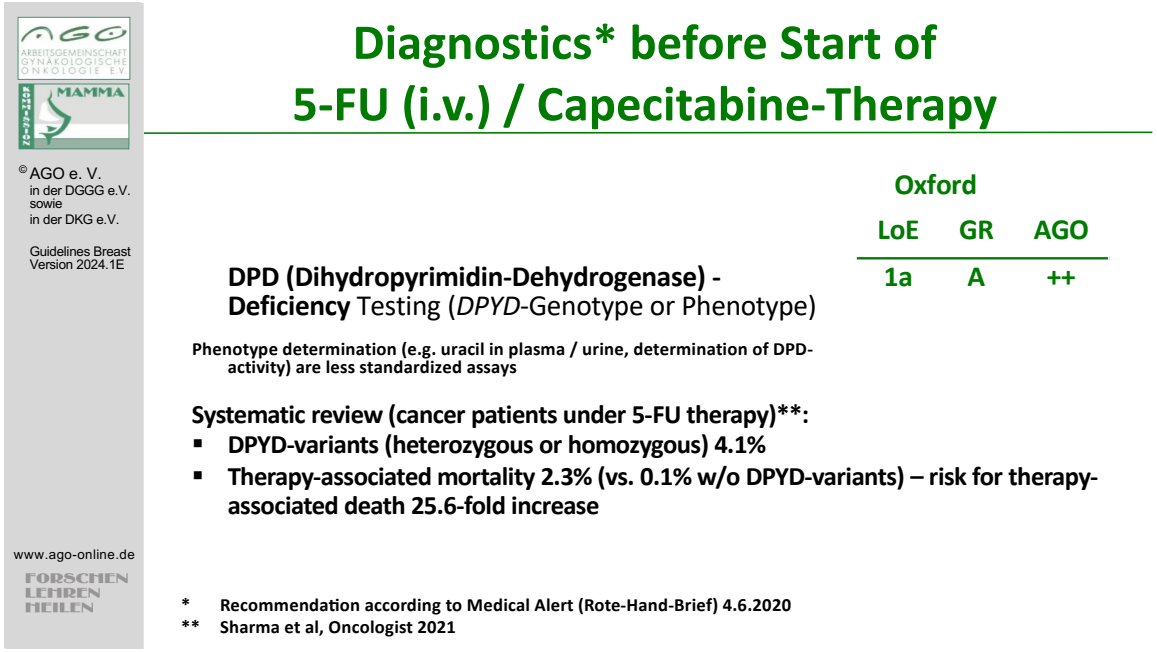



DPD Deficiency:

1. Rote-Hand-Brief vom 04.06.2020: https://www.bfarm.de/SharedDocs/Risikoinformationen/Pharmakovigilanz/DE/RHB/2020/rhb-fluorouracil.html (Zugriff am 17.01.2022)
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# Endocrine Therapy – Toxicities



Guidelines Breast
Version 2024.1E

www.ago-online.de

FORSCHEN
LEHREN
HEILEN

| | Tamoxifen | Anastrazole | Exemestane | Letrozole | Fulvestrant | Elacstrant |
|---|---|---|---|---|---|---|
| Infections / Infestations | - | - | - | 3 | 4 | - |
| Neoplasms (benin, malignant, unspecified) | 3 | - | - | - | - | - |
| Blood and lymphatic system disorders | 4 | - | 4 | 3 | 3 | - |
| Immune system disorders (allergies) | - | - | - | - | 4 | - |
| Endocrine disorders | 3 | - | - | - | - | 5 |
| Metabolism and nutrition disorders | 5 | 4 | 4 | 5 | 4 | 5 |
| Psychiatric disorders | - | 5 | 5 | 4 | - | 5 |
| Nervous system disorders | 4 | 5 | 4 | 4 | 4 | - |
| Eye disorders | 4 | 4 | - | 3 | - | - |
| Ear and lapyrinth disorders | - | - | - | - | - | - |
| Cardiac disorders | - | 4 | - | 3 | - | - |
| Vascular disorders (including hot flashes) | 4 | 5 | 5 | 5 | 4 | 5 |

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

Side effect categories- MedDRA (Medical Dictionary for Regulatory Activities)

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

Sources for product information (Download 19.01.2018)

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

Elacestrant: Fachinformation Elacestrant 2023

# Endocrine Therapy – Toxicities



| | Tamoxifen | Anastrazole | Exemestane | Letrozole | Fulvestrant | Elacstrant |
|---|---|---|---|---|---|---|
| Respiratory, thoracic and mediastinal disorders | 3 | - | - | 3 | - | - |
| Gastrointestinal disorders (nausea, emesis) | 5 | 5 | 5 | 4 | 5 | 5 |
| Hepatobiliary disorders | 4 | 4 | - | 3 | 5 | 4 |
| Skin and subcutis disorders (incl alopecia) | 5 | 5 | 5 | 5 | 4 | - |
| Musculosceletal and connective tissue | 4 | 5 | 5 | 5 | 4 | 5 |
| Renal and urinary disorders | - | - | - | 3 | 4 | - |
| Pregnancy, peurperal and perinatal disorders | - | - | - | - | - | - |
| Reproductive tract and breast disorders | 5 | 5 | - | 4 | 3 | - |
| General disorders / administration site conditions | 5 | 5 | 5 | 5 | 5 | - |
| Congenital, familiary and genetic disorders | 1 | - | - | - | - | - |
| Special features | * | ** | ** | ** | *** | |
| * Hot flushes; rarely endometrial cancer, thrombosis<br>** hot flashes, arthralgia, osteoporosis, cognition<br>***hot flushes | | | | | | |

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

Side effect categories- MedDRA (Medical Dictionary for Regulatory Activities)

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

Sources for product information (Download 19.01.2018)

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

# Key-Toxicities – Antibodies

| | Oxford LoE | Oxford GR |
|---|---|---|
| **Trastuzumab** | | |
| ▪ Cardiotoxicity in the adjuvant setting (1.0–2.0%) | 1b | A |
| ▪ Troponin I may identify patients at risk for cardiotoxicity | 2b | B |
| **Pertuzumab** | | |
| ▪ Skin rash, diarrhea, mucositis | 1b | A |
| **Bevacizumab** | | |
| ▪ Hypertension, proteinuria, bleeding, left ventricular dysfunction | 1a | A |

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
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Troponin I

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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.
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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
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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

# Toxicities of New Compounds: anti-HER2-TKI – Neratinib, Lapatinib –

## Lapatinib

| AE, % | All grades | Grade >/=3 |
|---|---|---|
| Diarrhea | 61% | 6% |
| Nausea | 18% | 4% |
| Rash | 60% | 6% |
| Fatigue | 16% | 4% |
| Cardiac | 3% | < 1% SAE |
| Hepatobiliary | 8% | |
| All AE % | 92% | SAE 6% |

## Neratinib

| AE, % | Alle Grade | Grad >/=3 |
|---|---|---|
| Diarrhea | 90 | 40,1 |
| Nausea | 43 | 2 |
| Abdominal pain | 36 | 2 |
| Fatigue | 27 | 2 |
| Emesis | 26 | 3 |
| Exanthema | 18 | 0,6 |
| Stomatitis | 14 | 0,6 |
| Appetite loss | 12 | 0,2 |
| Dyspepsia | 10 | 0,4 |
| ALAT elevated | 9 | 1,2 |
| ASAT elevated | 7 | 0,7 |
| Nail disorders | 8 | 0,3 |
| Dry skin | 6 | 0 |

| | LoE | GR | AGO |
|---|---|---|---|
| **Primary prophylaxis with loperamide** | 2b | B | ++ |

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
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3. Neratinib, Lapatinb s. aktuelle Fachinformation www. Fachinfo.de

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

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

1. Murthy RK, Loi S, Okines A, et al. Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer. N Engl J Med. 2020 Feb 13;382(7):597-609. doi: 10.1056/NEJMoa1914609. Epub 2019 Dec 11.
2. Tucatinib, Trastuzumab, Capecitabin s. aktuelle Fachinformation www. Fachinfo.de

# Key-Toxicities – Antibody-Drug-Conjugates

| | Oxford LoE | Oxford GR |
|---|---|---|
| **Sacituzumab Govitecan** | | |
| ▪ (Febrile) neutropenia, leukopenia, anemia, diarrhea, nausea, alopecia, fatigue | 1b | A |
| **Trastuzumab-Emtansin (T-DM1)** | | |
| Thrombozytopenia, elevation liver enzymes, pyrrexia, headache pneumonitis, neuropathy, fatigue | 1b | A |
| **Trastuzumab-Deruxtecan** | | |
| Interstitial lung disease, neuropenia, nausea, alopecia, fatigue | 1b | A |

Sacituzumab Govitecan…

1. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. N Engl J Med. 2021 Apr 22;384(16):1529-1541.
2. Rugo HS, Tolaney SM, Loirat D, et al. Safety analyses from the phase 3 ASCENT trial of sacituzumab govitecan in metastatic triple-negative breast cancer. NPJ Breast Cancer. 2022 Aug 29;8(1):98.

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
3. Barroso-Sousa R, Tarantino P, Tayob N et al. Cardiac outcomes of subjects on adjuvant trastuzumab emtansine vs paclitaxel in combination with trastuzumab for stage I HER2-positive breast cancer (ATEMPT) study (TBCRC033): a randomized controlled trial. NPJ Breast Cancer. 2022 Feb 16;8(1):18.
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Trastuzumab-Deruxtecan


1. Cortés J, Kim SB, Chung WP et al. Trastuzumab Deruxtecan versus Trastuzumab Emtansine for Breast Cancer. N Engl J Med. 2022 Mar 24;386(12):1143-1154.
2. Modi S, Jacot W, Yamashita T et al. Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer. N Engl J Med. 2022 Jul 7;387(1):9-20.
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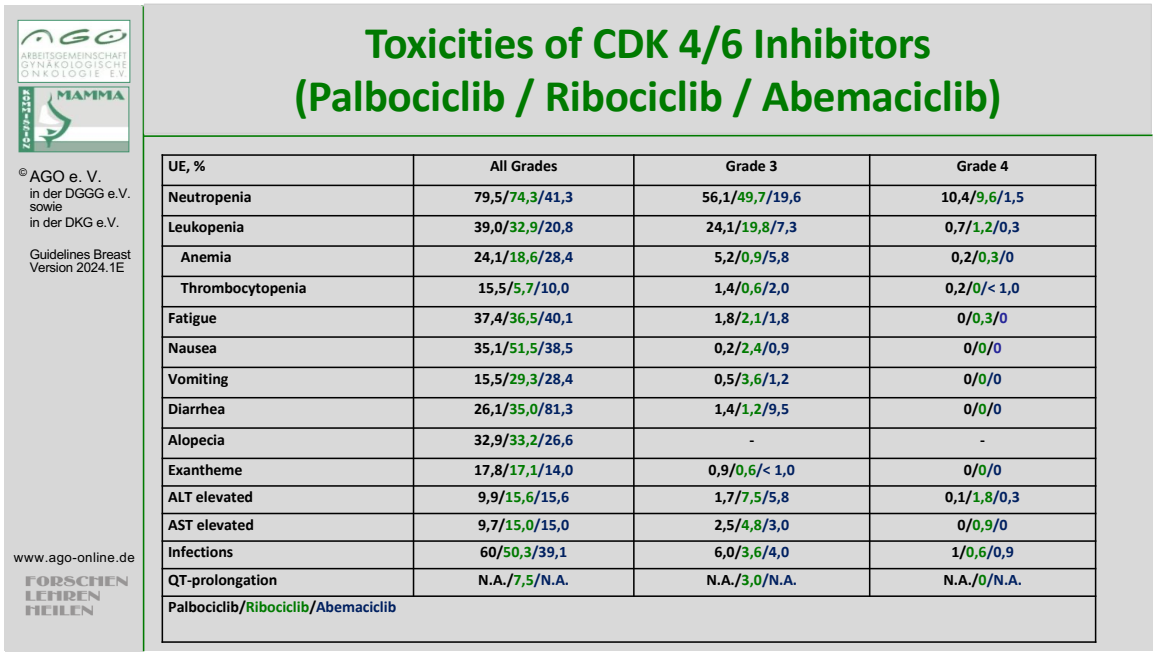


| UE, % | All Grades | Grade 3 | Grade 4 |
|---|---|---|---|
| Neutropenia | 79,5/74,3/41,3 | 56,1/49,7/19,6 | 10,4/9,6/1,5 |
| Leukopenia | 39,0/32,9/20,8 | 24,1/19,8/7,3 | 0,7/1,2/0,3 |
| Anemia | 24,1/18,6/28,4 | 5,2/0,9/5,8 | 0,2/0,3/0 |
| Thrombocytopenia | 15,5/5,7/10,0 | 1,4/0,6/2,0 | 0,2/0/< 1,0 |
| Fatigue | 37,4/36,5/40,1 | 1,8/2,1/1,8 | 0/0,3/0 |
| Nausea | 35,1/51,5/38,5 | 0,2/2,4/0,9 | 0/0/0 |
| Vomiting | 15,5/29,3/28,4 | 0,5/3,6/1,2 | 0/0/0 |
| Diarrhea | 26,1/35,0/81,3 | 1,4/1,2/9,5 | 0/0/0 |
| Alopecia | 32,9/33,2/26,6 | - | - |
| Exantheme | 17,8/17,1/14,0 | 0,9/0,6/< 1,0 | 0/0/0 |
| ALT elevated | 9,9/15,6/15,6 | 1,7/7,5/5,8 | 0,1/1,8/0,3 |
| AST elevated | 9,7/15,0/15,0 | 2,5/4,8/3,0 | 0/0,9/0 |
| Infections | 60/50,3/39,1 | 6,0/3,6/4,0 | 1/0,6/0,9 |
| QT-prolongation | N.A./7,5/N.A. | N.A./3,0/N.A. | N.A./0/N.A. |
| Palbociclib/Ribociclib/Abemaciclib | | | |


Palbociclib

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Ribociclib

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Abemaciclib

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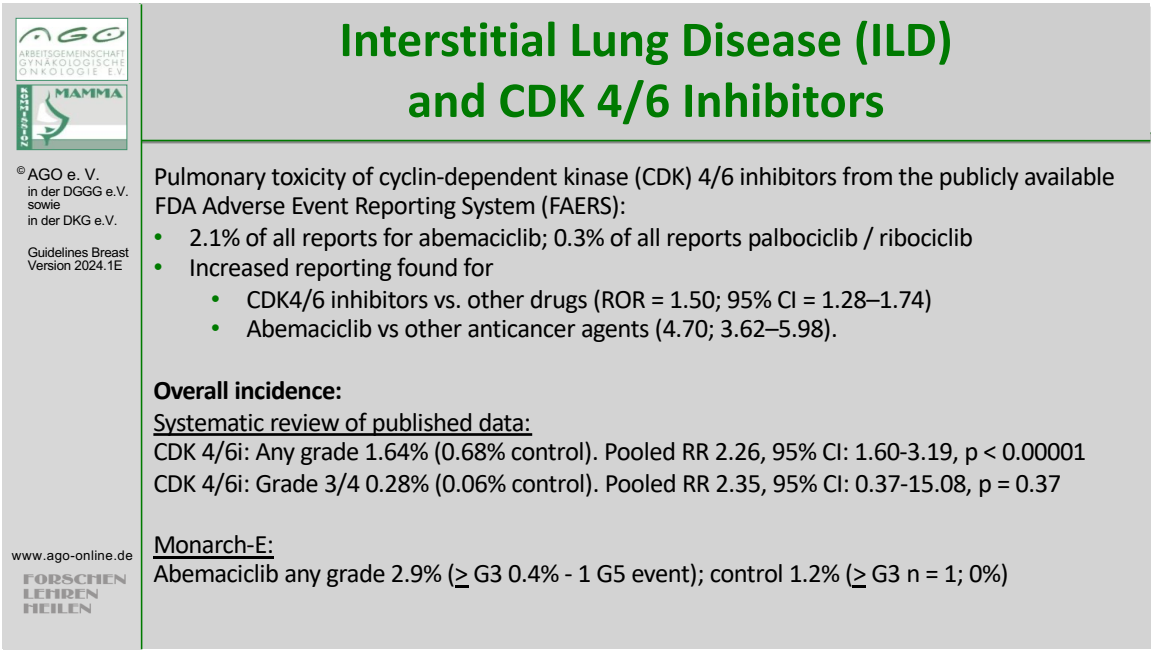



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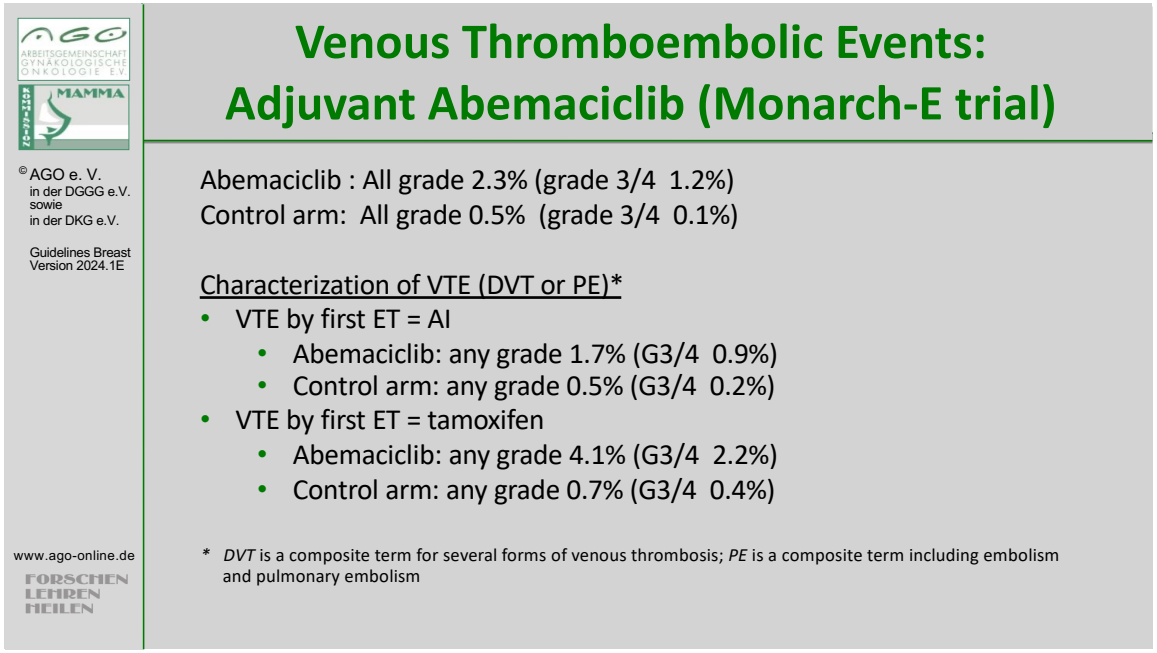



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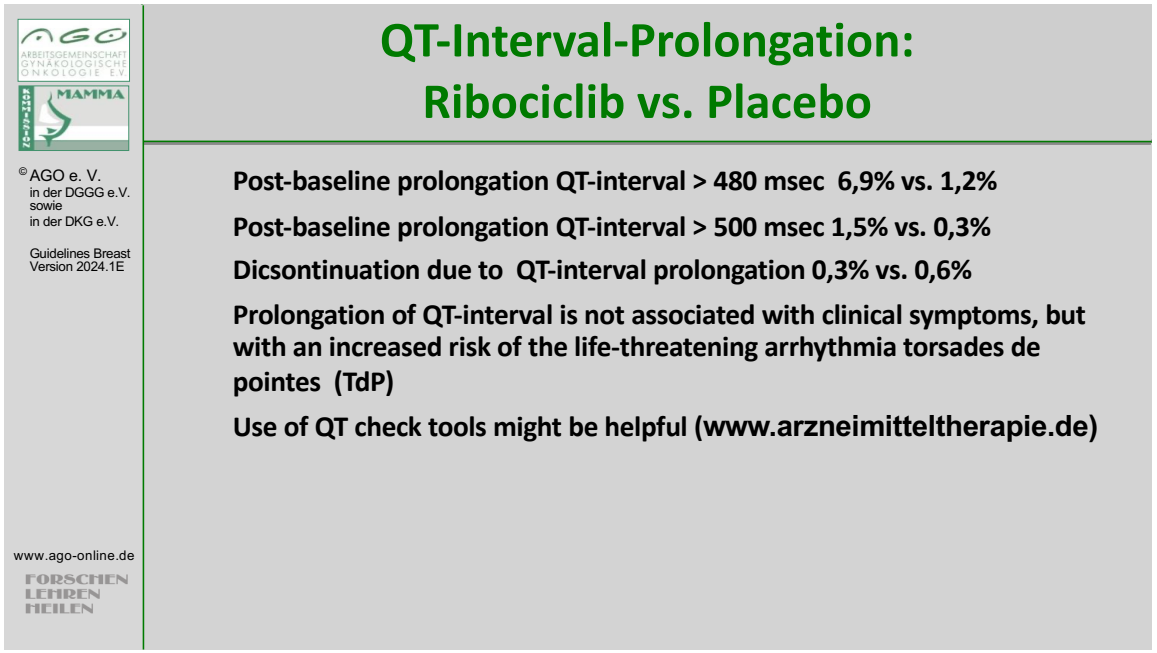



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# Toxicities of mTOR-Inhibitor (Everolimus)



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

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

# Toxicities of PI3K Inhibitor Alpelisib in Combination with Endocrine Therapy

**Alpelisib + Fulvestrant**

| UE, % | All Grade | Grad >/=3 |
|---|---|---|
| Hypergycemia | 63,7% | 32,7% |
| Diarrhea | 57,7% | 6,7% |
| Nausea | 44,7% | 2,5% |
| Decreased appetite | 35,6% | < 1% SAE |
| Rush | 35,5% | 9,9% |
| Vomiting | 27,1% | < 1% SAE |
| Weight loss | 26,8% | 3,9% |
| Stomatitis | 24,6% | 2,5% |
| Fatique | 24,3% | 3,5 |
| Asthenia | 20,4% | 1,8 |
| Alopecia | 19,7% | 0 |
| Mucositis | 18,3% | 2,1 |

**Regard recommendations for management of side effects (Diabetes mellitus, hyperglycemia, Insulin resistance und metabolic syndrom)**

| LoE | GR | AGO |
|---|---|---|
| 2b | B | ++ |

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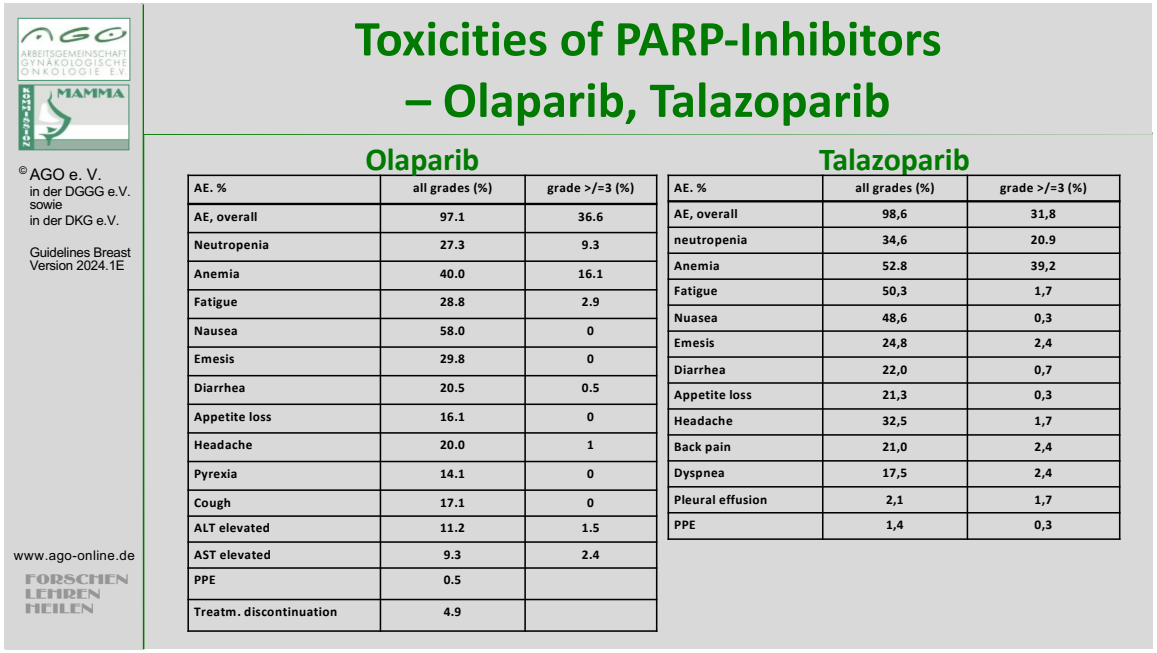



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2. Robson M, Im SA, Senkus E et al. Olaparib for metastatic breast cancer in patients with germline BRCA mutation N Engl J Med 377: 523-533, 2017

# Immune Checkpoint Inhibitors

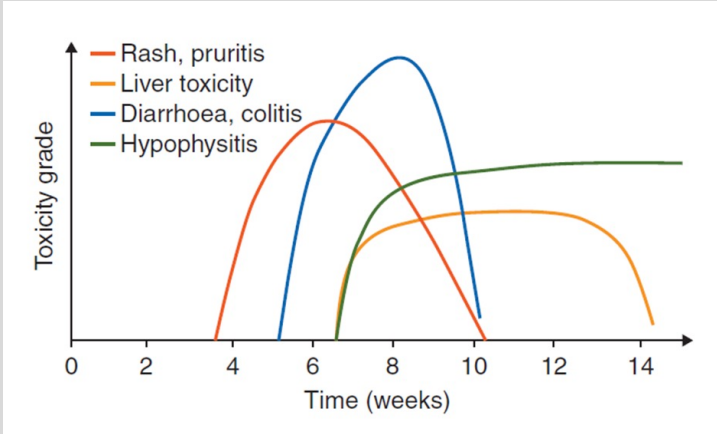
- **Therapeutic approaches (antibodies)**
  - **PD-1 / PD-L1**

    **PD-1**
    - **Nivolumab**
    - **Pembrolizumab**

    **PD-L1**
    - **Atezolizumab**
    - **Durvalumab**
    - **Avelumab**

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

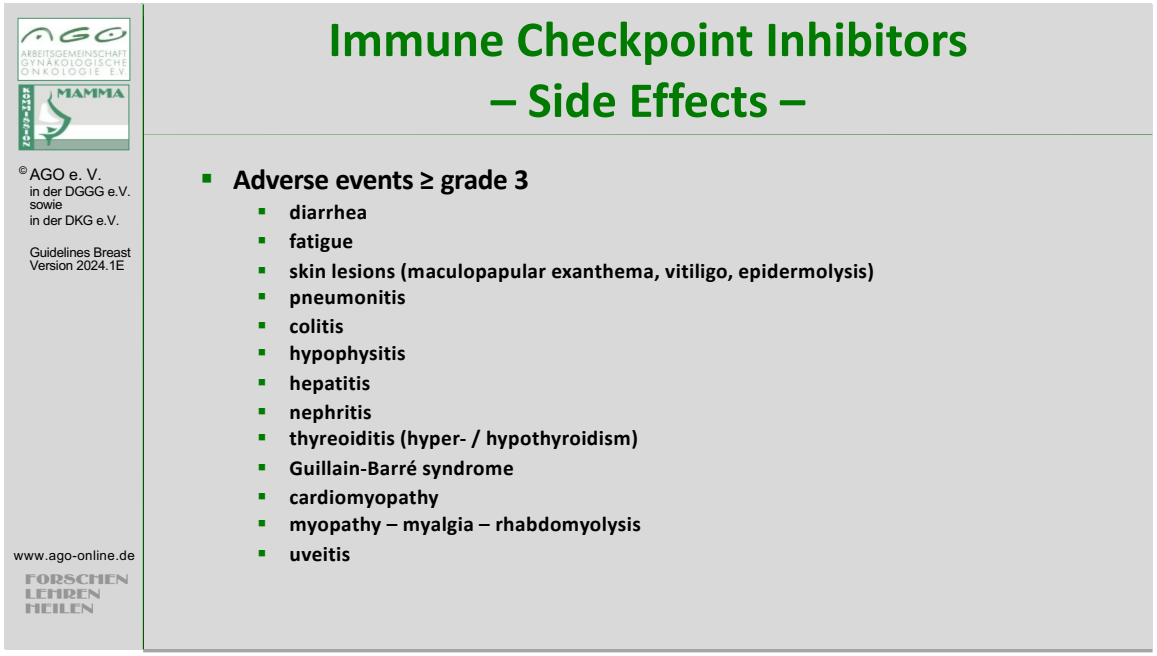
## Immune Checkpoint Inhibitors
## Time Course of Adverse Events, e.g. Ipilimumab




*Haanen J et al. Ann Oncol 2017; 28 (suppl 4): 119-142*



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

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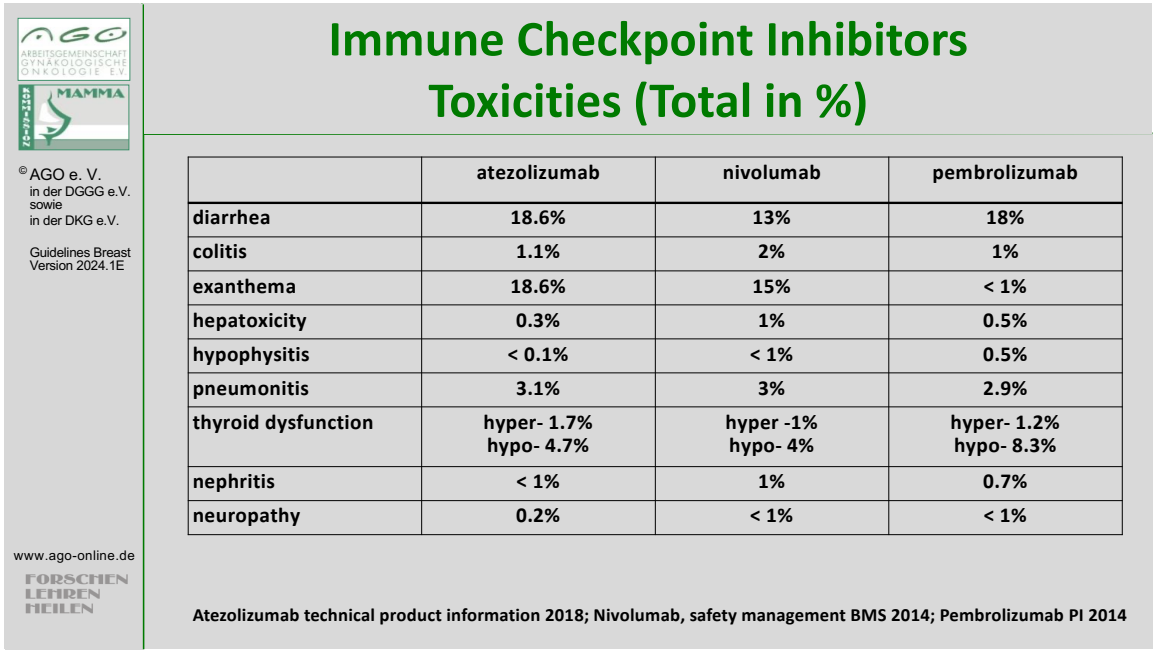
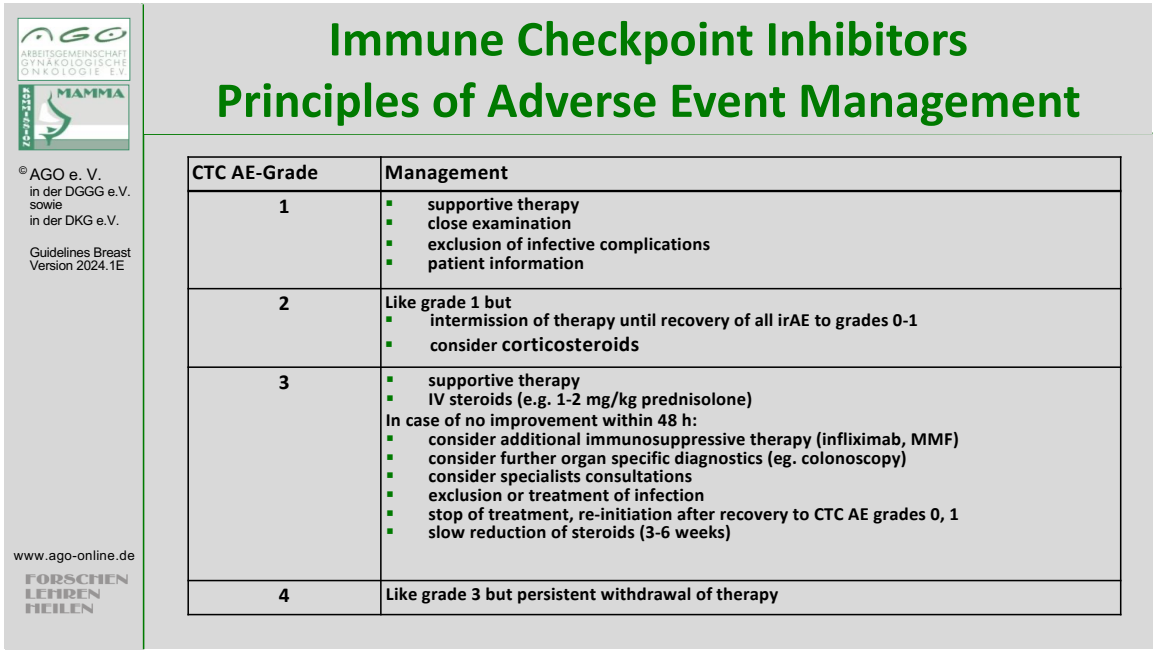



| | atezolizumab | nivolumab | pembrolizumab |
|---|---|---|---|
| diarrhea | 18.6% | 13% | 18% |
| colitis | 1.1% | 2% | 1% |
| exanthema | 18.6% | 15% | < 1% |
| hepatoxicity | 0.3% | 1% | 0.5% |
| hypophysitis | < 0.1% | < 1% | 0.5% |
| pneumonitis | 3.1% | 3% | 2.9% |
| thyroid dysfunction | hyper-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

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




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


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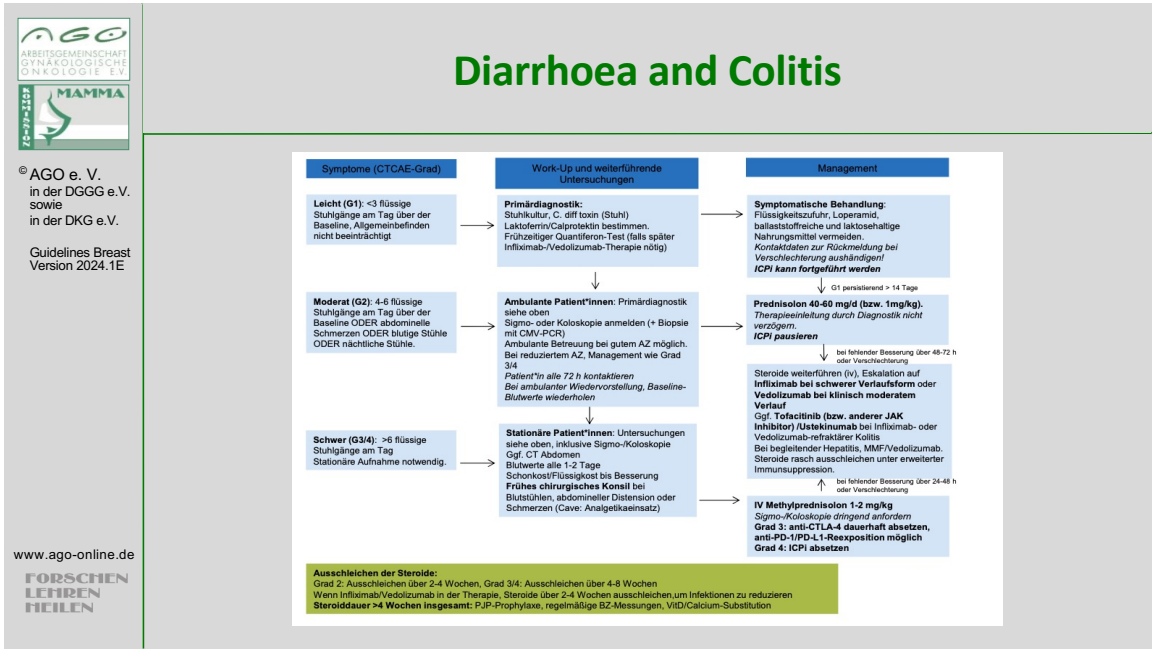



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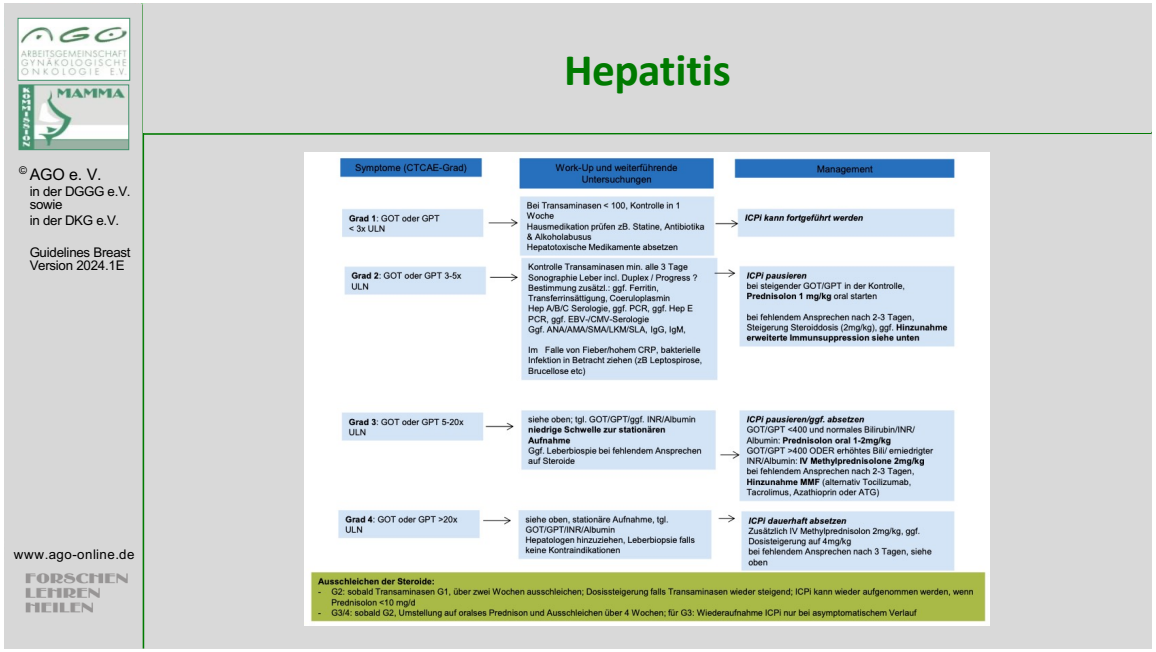


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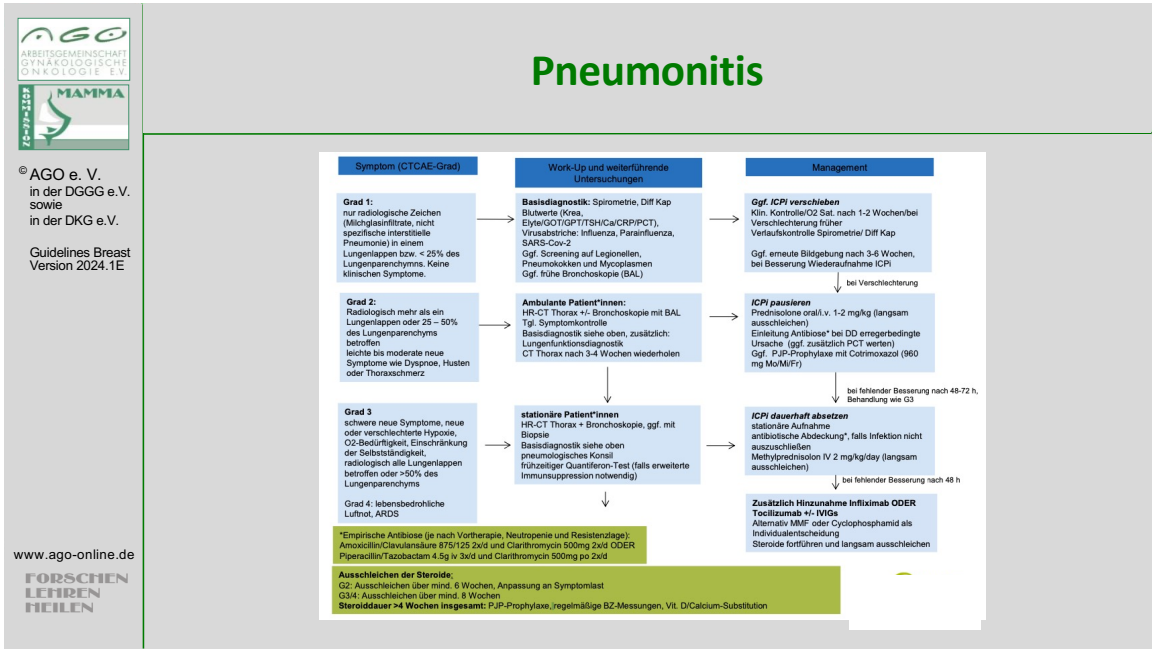



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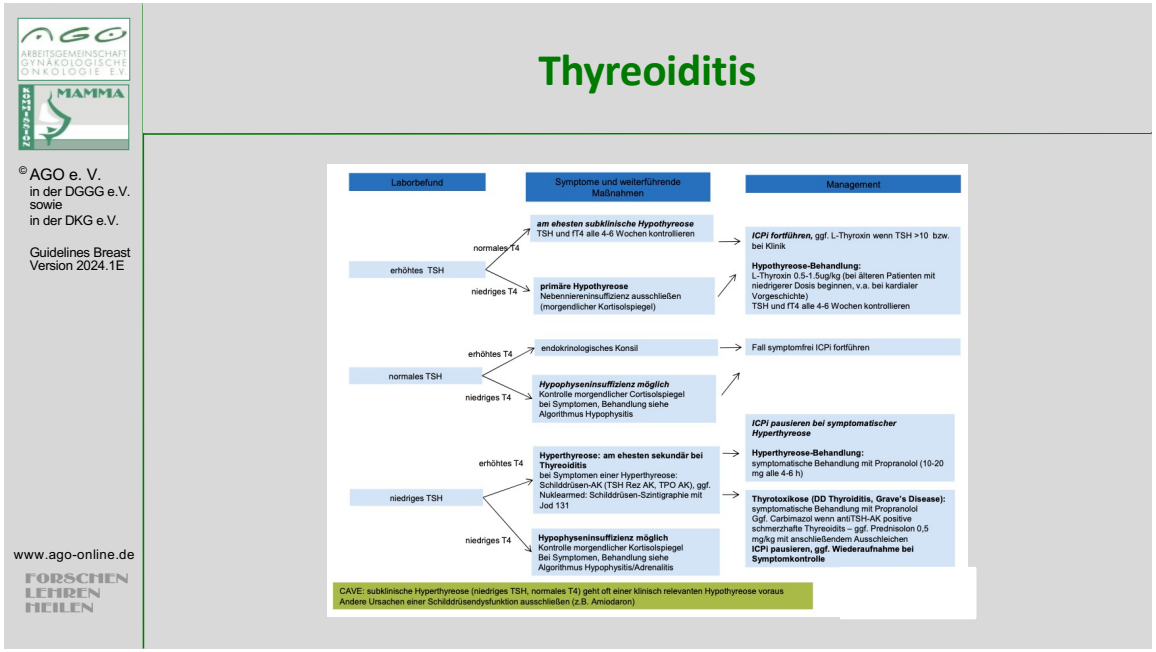



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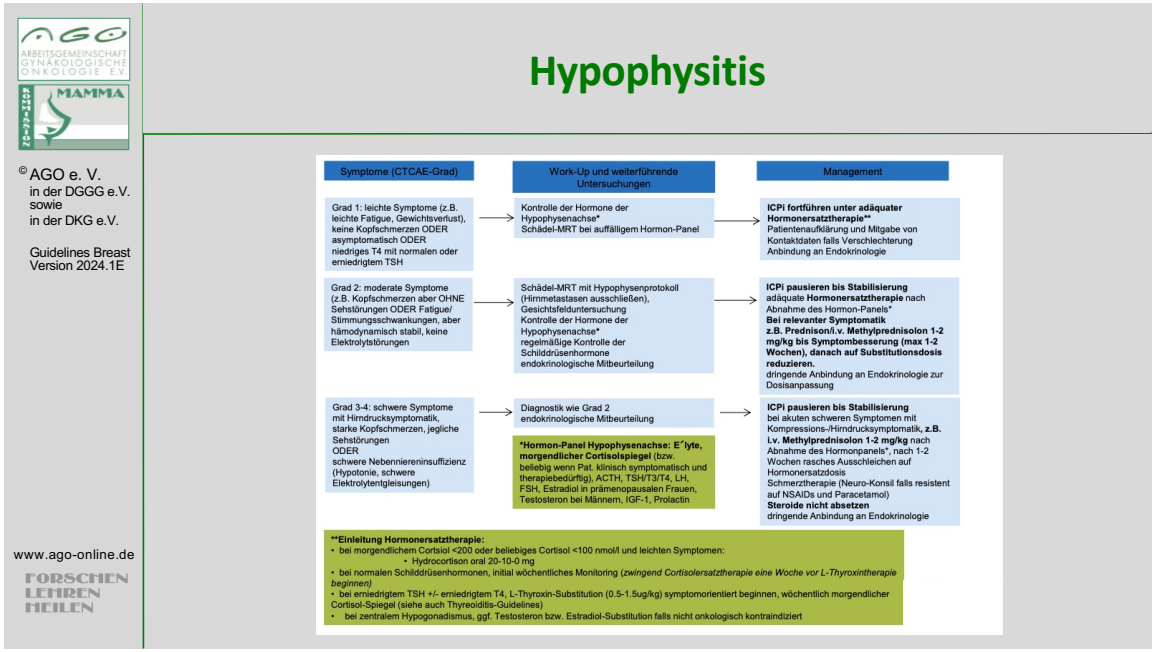



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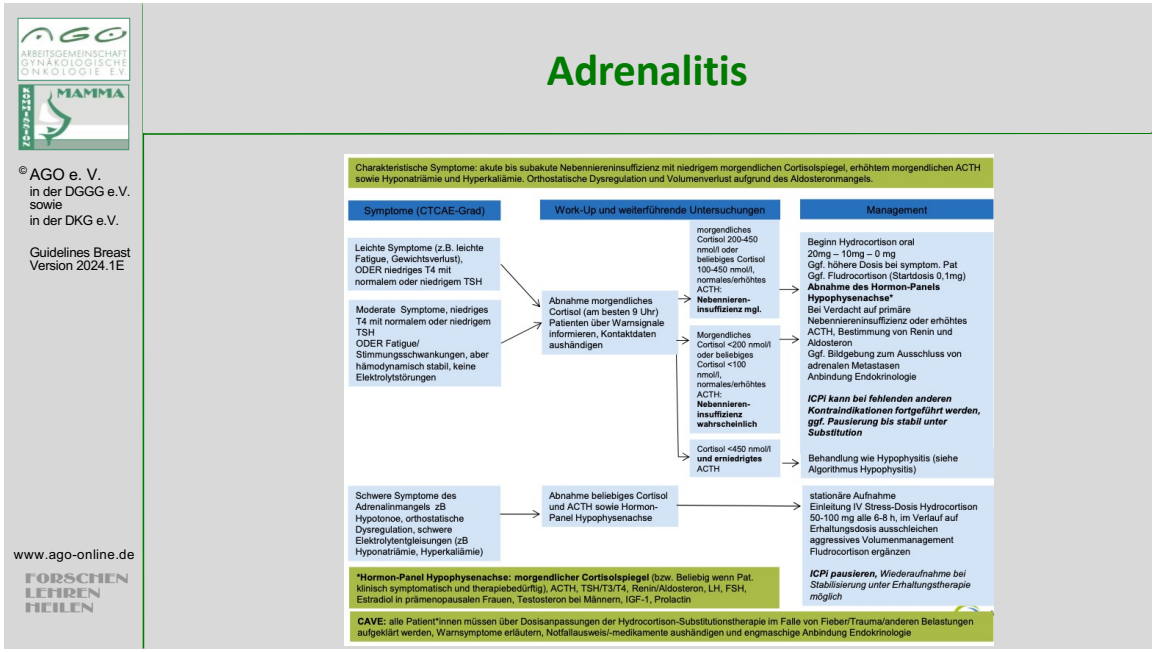



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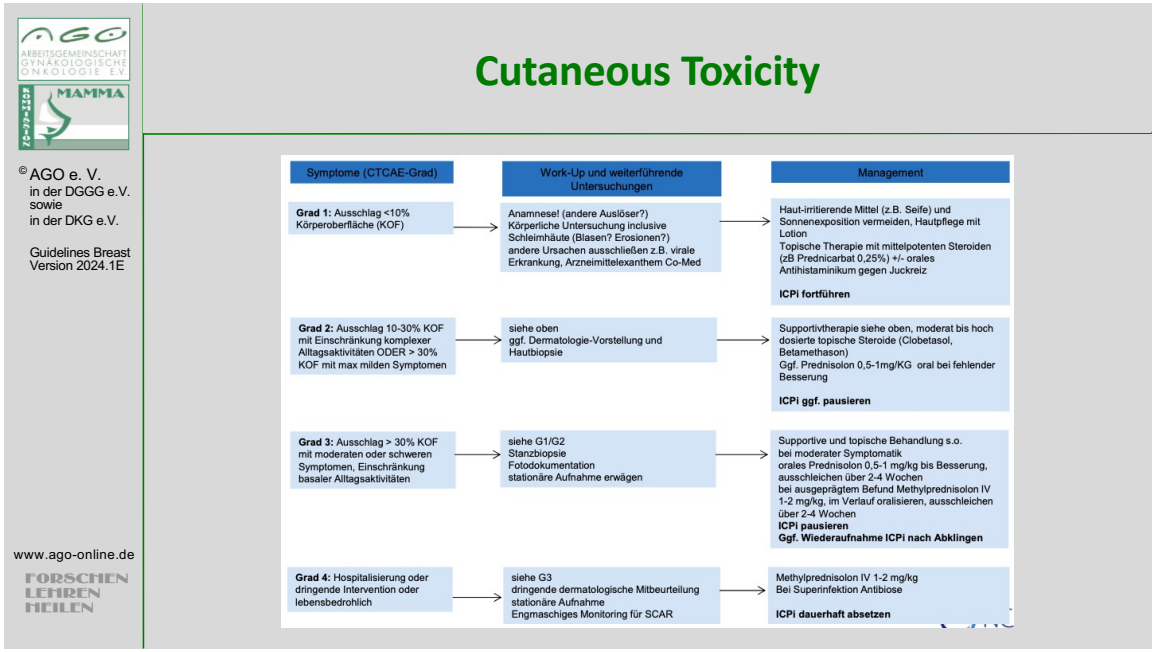



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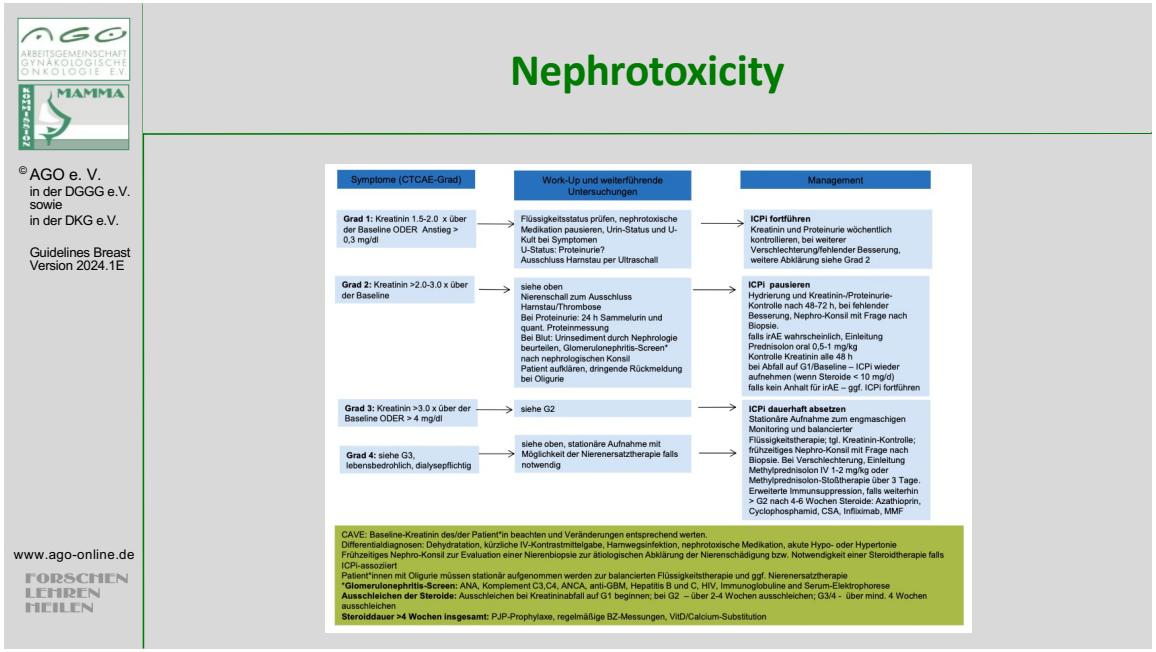



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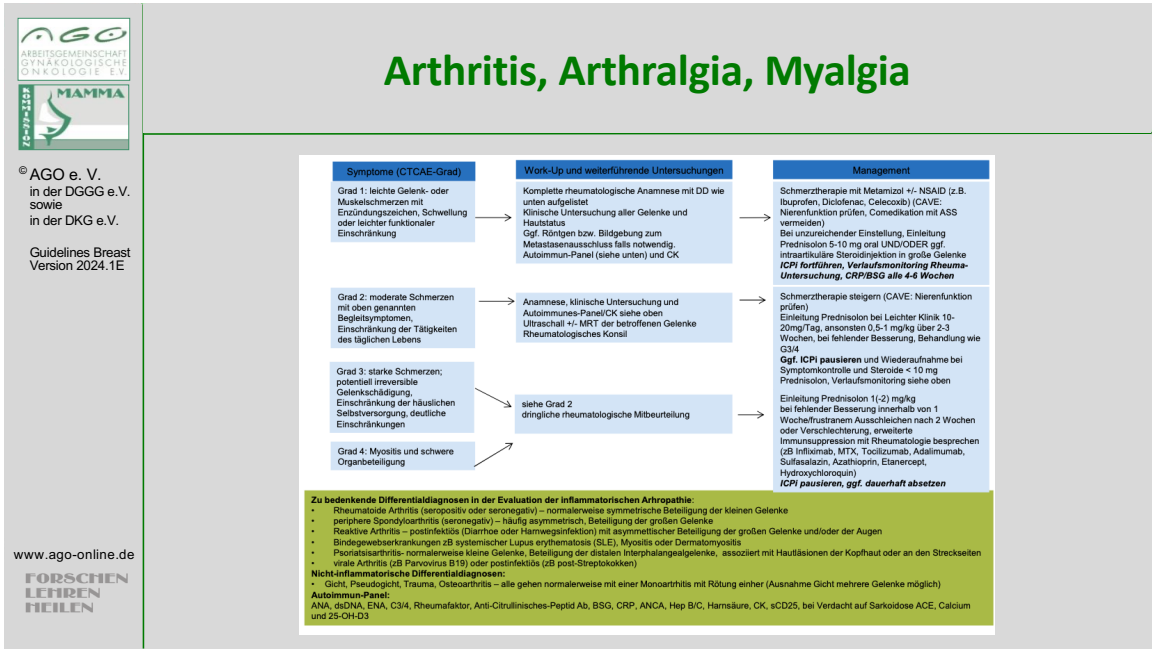



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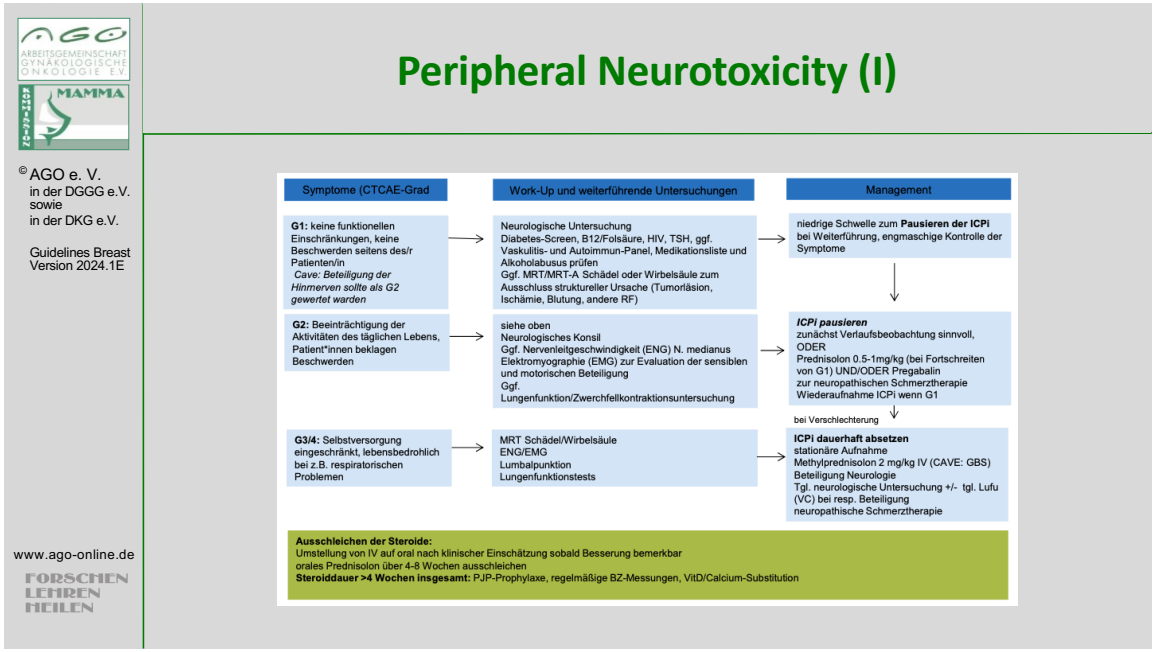



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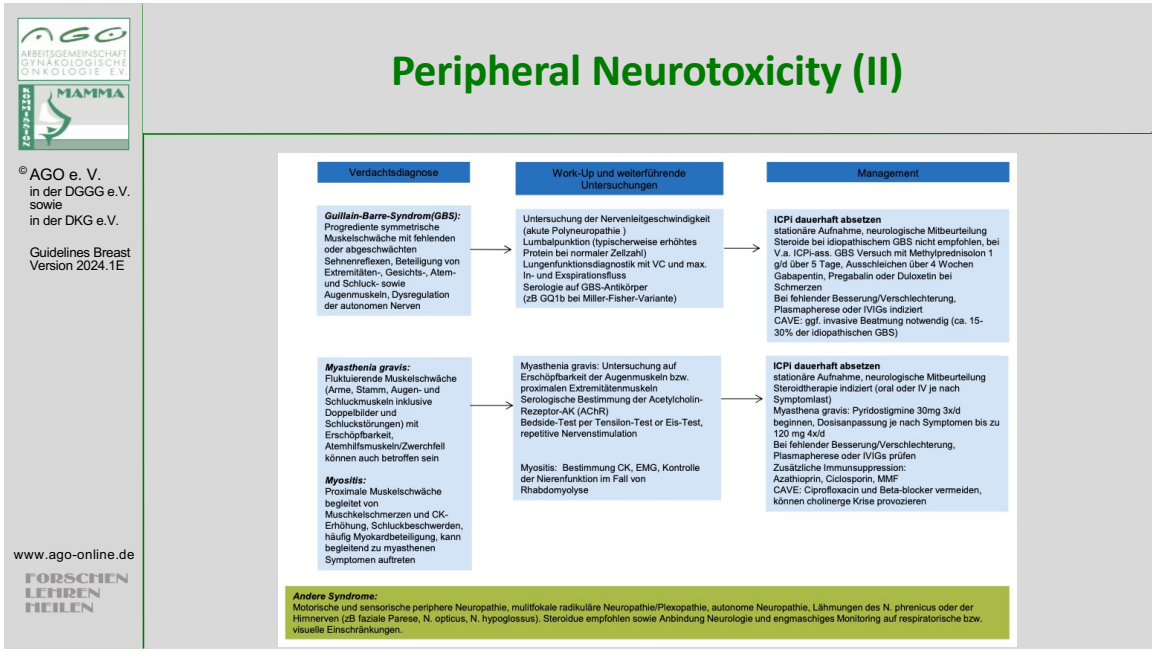



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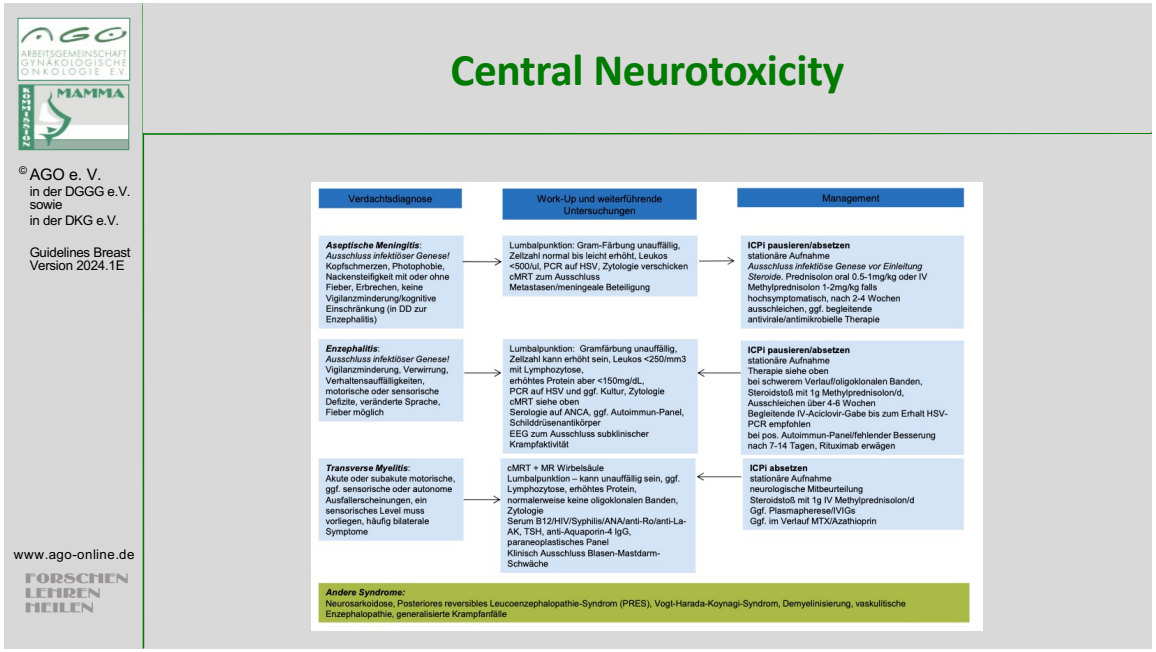



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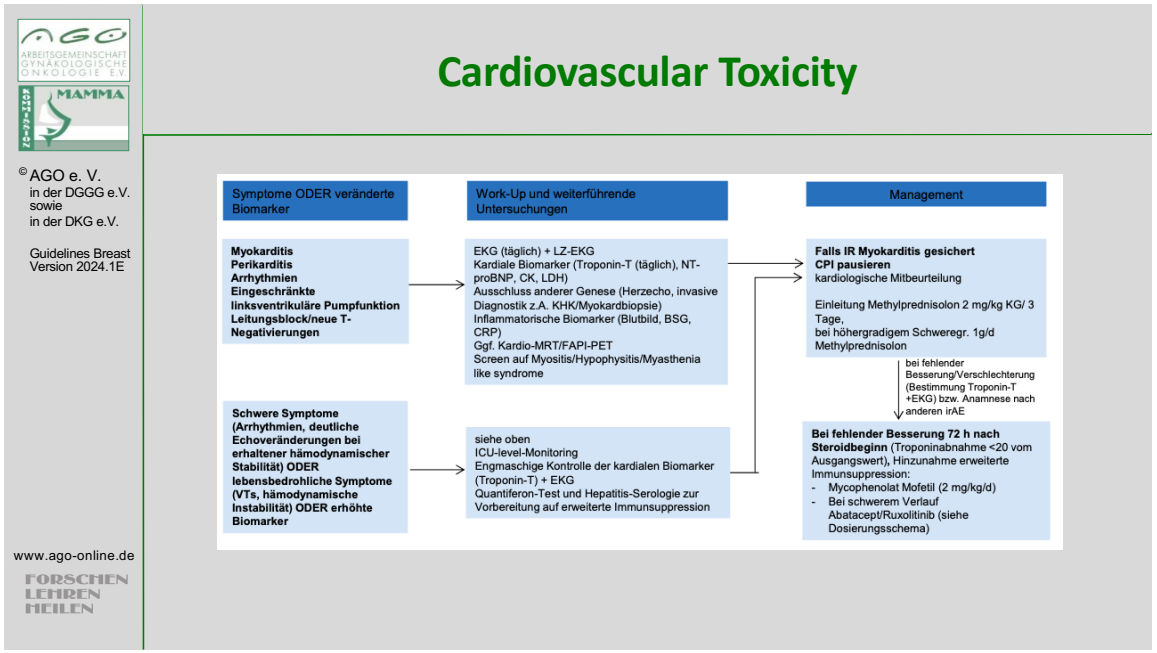



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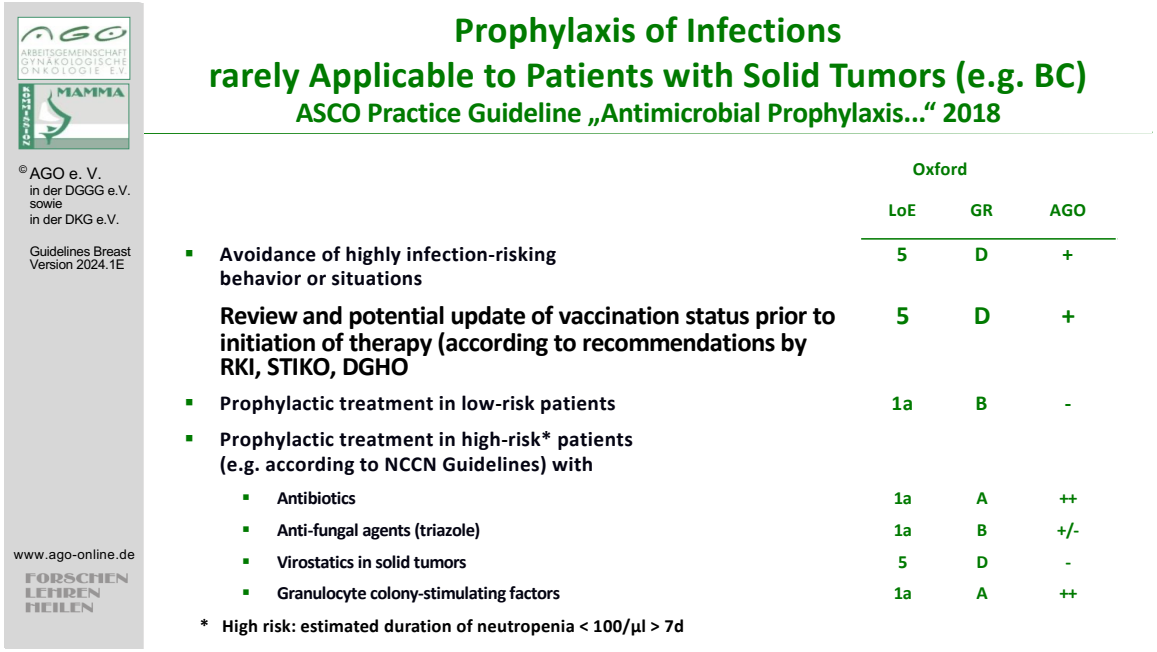
# Side Effects According Organ Systems
## Incidence, Prevention, Therapy

## 1. Infections

- **General prophylaxis for infections**
- **Hepatitis B virus screening**
- **Covid-19 (see joint guidelines with DGHO)**

1. Hwang JP, Feld JJ, Hammond SP, et al. Hepatitis B Virus Screening and Management for Patients With Cancer Prior to Therapy: ASCO Provisional Clinical Opinion Update. J Clin Oncol 2020;38:3698-3715.
2. Giesen N, Sprute R, Rüthrich M et al. 2021 update of the AGIHO guideline on evidence-based management of COVID-19 in patients with cancer regarding diagnostics, viral shedding, vaccination and therapy. COVID-19 guideline panel of the Infectious Diseases Working Party (AGIHO) of the German Society for Haematology and Medical Oncology (DGHO). Eur J Cancer. 2021 Apr;147:154-160.

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Guidelines Breast
Version 2024.1E



# Hepatitis B Virus Screening before Chemotherapy

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ **Hepatitis B virus screening before adjuvant chemotherapy (HBsAG, anti-HBC, anti-HBs)** | 2c | B | + |
| **In case of positive serology or reactivation:** | | | |
| ▪ **Prophylactic therapy with virustatic drugs if HBV-DNA detected (according AGIHO / DGHO – recommendations)** | 1b | A | ++ |
| ▪ **Hepatitis C virus screening before chemotherapy** | 5 | D | +/- |

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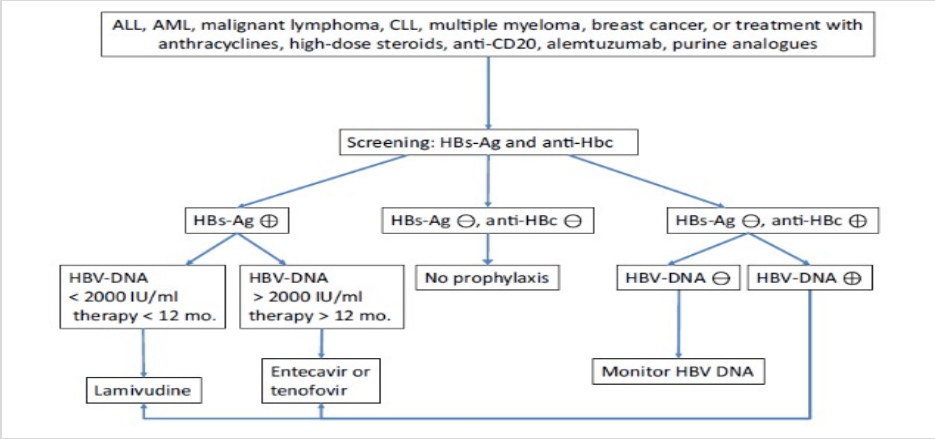
# AGIHO / DGHO – Recommendations on Hepatitis B Virus Screening in Oncology



Guidelines Breast
Version 2024.1E

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# Side Effects According Organ Systems
## Incidence, Prevention, Therapy

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


# Secondary Malignancies I

| | Oxford LoE | Oxford GR |
|---|---|---|
| ▪ With regard to solid tumors, chemotherapy induced secondary malignancies are rare events | 2a | |
| ▪ Alkylating agents increase the risk of leukemia dose- dependently to a total of 0.2–0.4% within 10–15 years | 2a | |
| ▪ Anthracycline-containing regimens increase the risk of MDS and leukemia to 0.2–1.7% within 8 to 10 years | 2a | |
| ▪ PARP-inhibitors are associated with an increased risk of AML and MDS to 0.5–1% | 2b | |
| ▪ Radiotherapy increases the risk of leukemia by 0.2–0.4% in patients treated with anthracycline-containing chemotherapy | 2b | |
| ▪ Tamoxifen approximately doubles the risk for developing endometrial cancer (in pts. older than 55 yrs. at start of therapy) | 2b | |


Statements 1-5

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.
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Tamoxifen and endometrial cancer

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# Secondary Malignancies II (After Radiotherapy)

| | Oxford LoE |
|---|---|
| ▪ **Radiotherapy (PMRT, BET) may moderately enhance the risk of ipsilateral lung cancer and angiosarcoma (10-15/10.000) 5–10 years after treatment** | 1a |
| ▪ **Enhanced risk especially among ever smokers** | 2b |
| ▪ **No difference of secondary malignancy between PBI und WBI** | 2c |

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# Side Effects According Organ Systems
## Incidence, Prevention, Therapy

### 3. Blood and Lymphatic System Disorders

- Anemia
- Neutropenia
- Febrile Neutropenia (FN)

# Anemia – Indications for Therapy with Erythropoiesis-stimulating Agents (ESAs)

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ Indicated in asymptomatic anemia | 1a | B | - |
| ▪ Therapy and secondary prophylaxis in CTx-induced anemia | 1a | A | + |
| ▪ Adjuvant setting | 1b | A | + |
| ▪ Neoadjuvant / metastatic setting | 1a | A | +/- |
| ▪ In dose-dense / dose-escalated CTx (iddETC) | 1b | A | + |
| ▪ Treatment start at Hb-levels < 10 g/dL | 1a | A | + |
| ▪ Target Hb 11–12 g/dL | 1a | A | + |
| ▪ Improvement of outcome (DFS, OS) | 1a | B | -- |
| ▪ Risk of thromboembolic events is increased by use of ESAs | 1a | A | |

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

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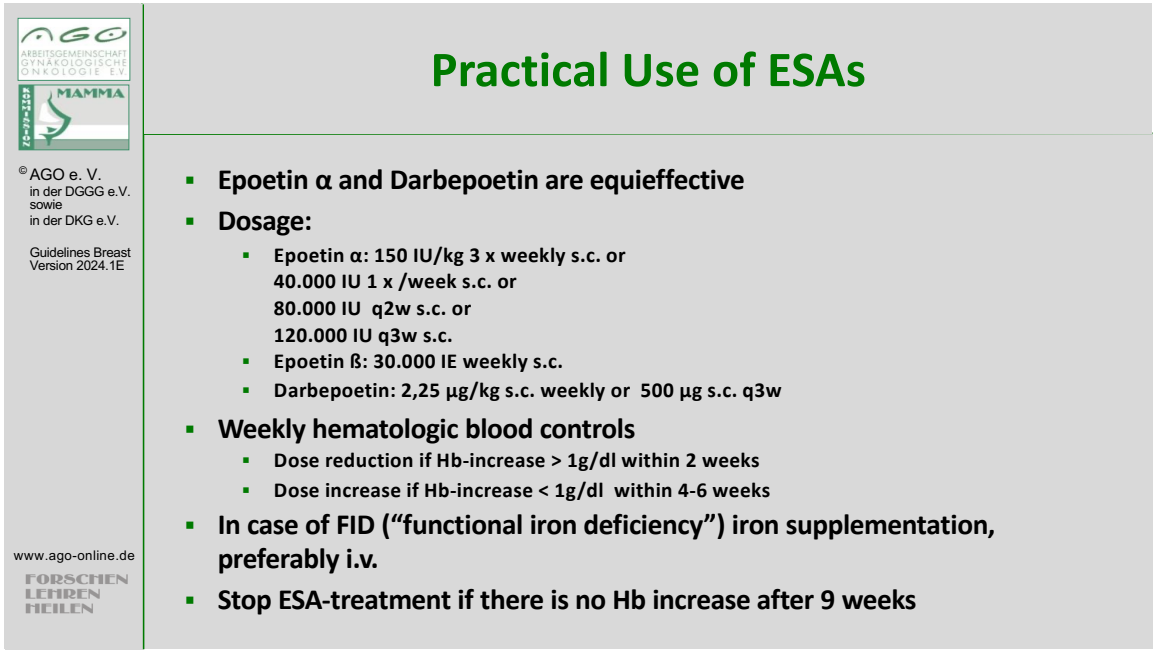



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<u>Relevant guidelines</u>


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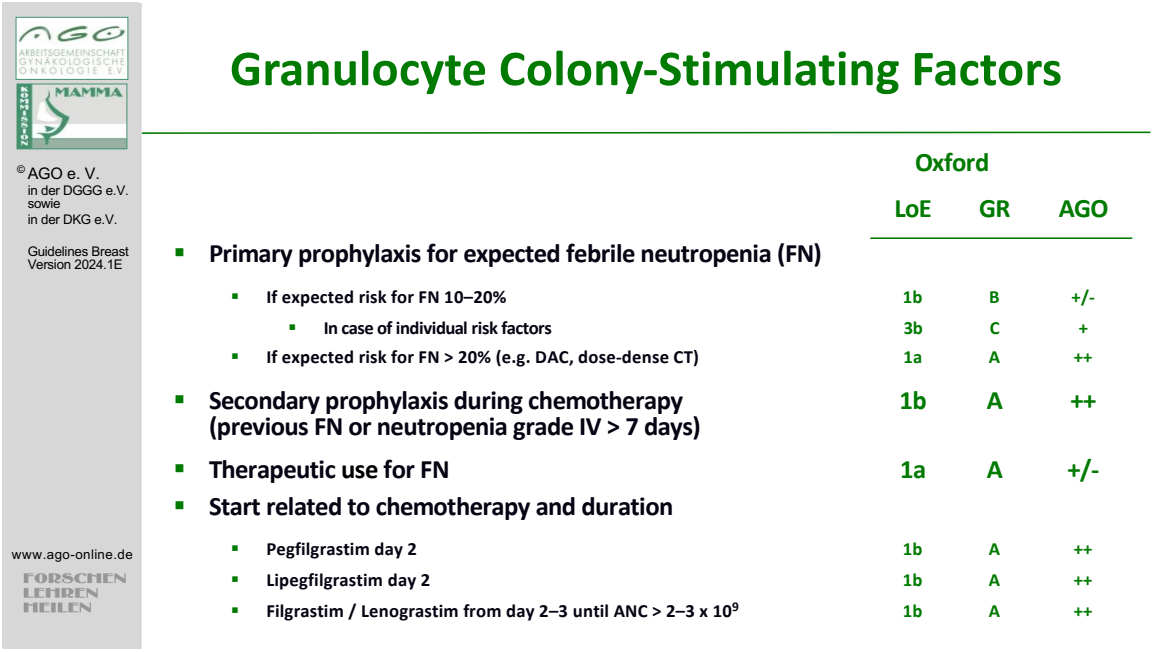


## Granulocyte Colony-Stimulating Factors

| | Oxford LoE | Oxford GR | AGO |
|---|---|---|---|
| ▪ **Primary prophylaxis for expected febrile neutropenia (FN)** | | | |
| ▪ If expected risk for FN 10–20% | 1b | B | +/- |
| ▪ In case of individual risk factors | 3b | C | + |
| ▪ If expected risk for FN > 20% (e.g. DAC, dose-dense CT) | 1a | A | ++ |
| ▪ **Secondary prophylaxis during chemotherapy (previous FN or neutropenia grade IV > 7 days)** | **1b** | **A** | **++** |
| ▪ **Therapeutic use for FN** | **1a** | **A** | **+/-** |
| ▪ **Start related to chemotherapy and duration** | | | |
| ▪ Pegfilgrastim day 2 | 1b | A | ++ |
| ▪ Lipegfilgrastim day 2 | 1b | A | ++ |
| ▪ Filgrastim / Lenograstim from day 2–3 until ANC > 2–3 x $10^9$ | 1b | A | ++ |


Relevante Leitlinien

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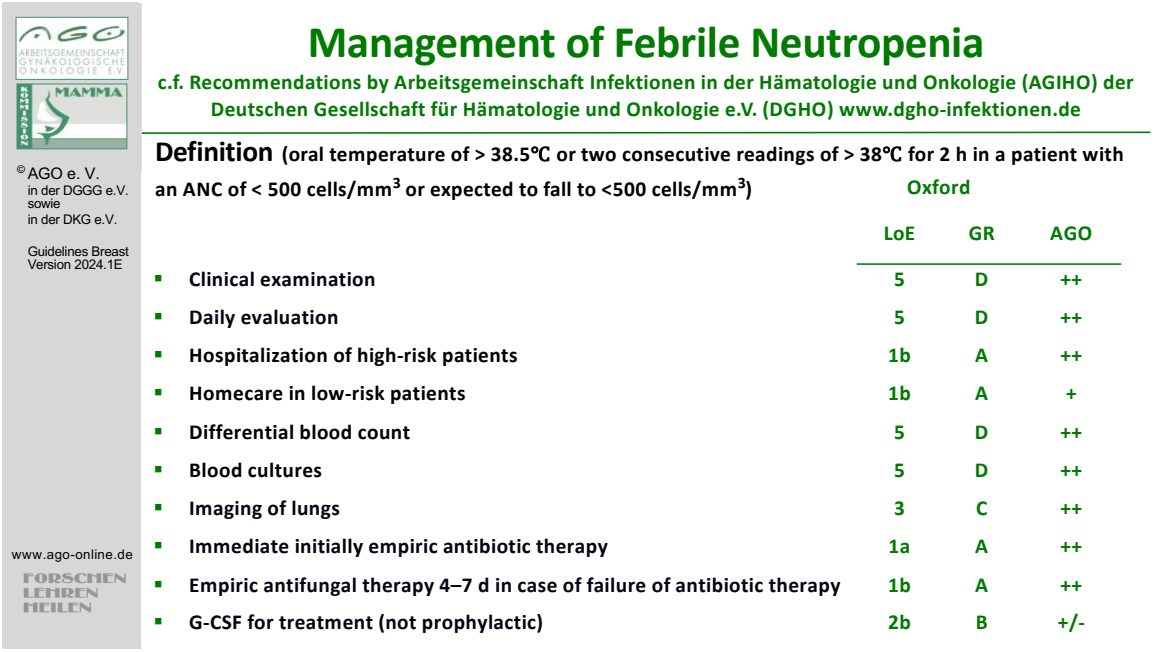



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S3-Leitlinie: Supportive Therapie:

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   Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3 – Februar 2020
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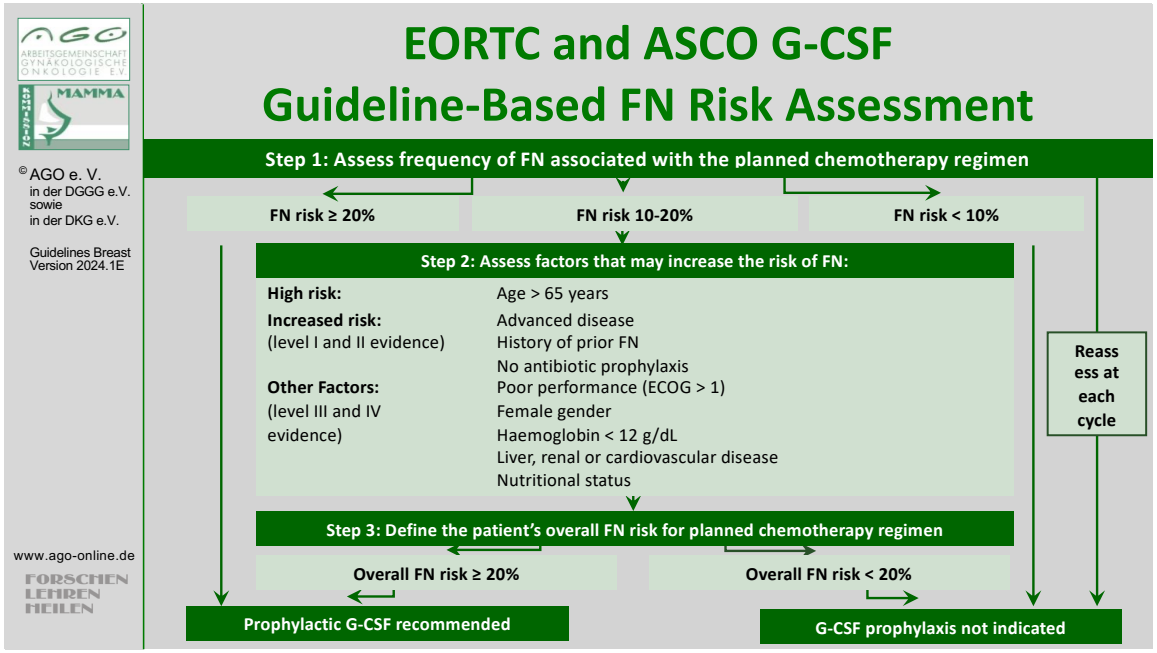



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Guidelines Breast
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# 4. Toxicities / Ovaries

| Therapy-associated amenorrhea (CRA, CIA, TIA) | Oxford LoE |
|---|---|
| ▪ CRA may be permanent or temporary (depending on age of the patient and type of chemotherapy) | 2b |
| ▪ The risk of CRA increases with patient's age and duration of the chemotherapy | 2b |
| ▪ CRA is an imperfect surrogate for menopause and fertility | 5 |
| ▪ Adjuvant endocrine therapy with GnRHa induces reversible amenorrhea, but delays conception to a less fertile period | 5 |
| ▪ Ovarian reserve of women who remain premenopausal after CTX is reduced | 2b |
| ▪ CRA is associated with improved outcome (DFS / OS) | 1b |

Synonym: Chemotherapy related or induced / Treatment induced Amenorrhea (CRA, CIA, TIA)

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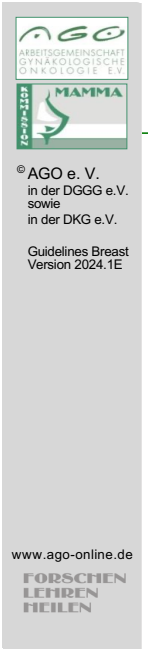
# Side Effects According Organ Systems
## Incidence, Prevention, Therapy

## 5. Psychiatric Disorders

- Depression
- Fatigue
- Cognitive impairment
- Sleep disturbances




# (Therapy-associated) Depression

| | Oxford LoE | Oxford GR | AGO |
|---|---|---|---|
| ▪ **Depression is an often reported adverse event in breast cancer patients (20–30%)** | 2a | B | |
| ▪ **Psychological interventions are effective to improve mood, but not survival in distressed and depressed patients** | 1b | A | |
| ▪ **Antidepressants have shown to improve depression in breast cancer patients** | 1b | A | |
| ▪ **Regular exercise participation can prevent depression in breast cancer survivors** | 2b | B | + |

Statements 1-4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# (Therapy-related) Fatigue

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ Fatigue frequent in breast cancer patients (30–60%) | 2a | B | |
| ▪ Exclusion of somatic reasons (anemia, tumor burden, co-morbidity, medication) for fatigue | 1a | A | ++ |
| ▪ Psycho-social interventions specifically addressing fatigue efficient in reducing fatigue | 1a | A | ++ |
| ▪ Physical exercise can improve fatigue | 1b | D | + |
| ▪ Yoga can improve fatigue | 2b | B | + |
| ▪ Methylphenidate or corticosteroids (short-term) can improve fatigue | 1a | D | + |

Guideline:

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# (Therapy-associated) Cognitive Impairment

| | Oxford LoE | Oxford GR |
|---|---|---|
| ▪ **Therapy-related cognitive deficits ("chemobrain") frequently described (16–75%)** | 2a | B |
| ▪ **Cognitive-behavioral therapy beneficial for cognitive function** | 2b | B |
| ▪ **Methylphenidate may improve cognitive function in cancer patients** | 3a | C |
| ▪ **Under therapy with aromatase inhibitors, deterioriation of cognitive performance was observed (espec. verbal memory)** | 1a | B |

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

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

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# (Therapy-associated) Sleep Disturbances

| | Oxford LoE | GR | AGO |
|---|---|---|---|
| ▪ **Sleep disturbances are a common problem in breast cancer patients during and after therapy (20–70%)** | 2a | B | |
| ▪ **Behavioral therapies demonstrated efficacy in treatment of insomnia and improved quality of life** | 1b | A | ++ |

Sleep disturbances are a common problem….

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Behavioral therapies have demonstrated efficacy…..

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Guidelines Breast
Version 2024.1E

## 6. Nervous system disorders

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

# Chemotherapy-Induced Peripheral Neuropathy (CIPN)

- **Incidence with taxanes:**
  - **Grade 1–2: 20–50%**
  - **Grade 3–4: 6–20%**
- **Risk factors: type and dose of chemotherapy, BMI, reduced physical activity**
- **Individual risk factors**
  - **Diabetes mellitus**
  - **Nutritive-toxic compounds part. alcohol**
  - **Renal failure**
  - **Hypothyreosis**
  - **Collagenoses / vasculitis**
  - **Vitamine deficiency**
  - **HIV-Infection**
  - **CMT-Gen mutations**

**Unclear:**

- **Other genetic factors (SNPs, mutations)**

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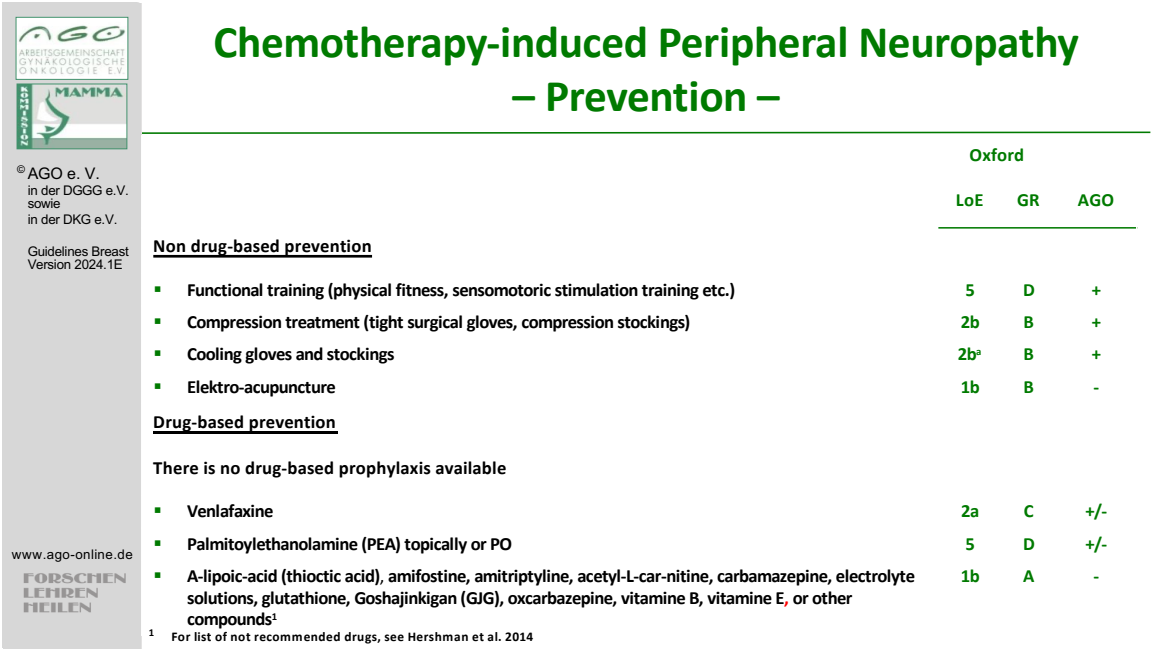


## Chemotherapy-induced Peripheral Neuropathy – Prevention –

| | Oxford LoE | GR | AGO |
|---|---|---|---|
| **Non drug-based prevention** | | | |
| ▪ Functional training (physical fitness, sensomotoric stimulation training etc.) | 5 | D | + |
| ▪ Compression treatment (tight surgical gloves, compression stockings) | 2b | B | + |
| ▪ Cooling gloves and stockings | 2b[a] | B | + |
| ▪ Elektro-acupuncture | 1b | B | - |
| **Drug-based prevention** | | | |
| There is no drug-based prophylaxis available | | | |
| ▪ Venlafaxine | 2a | C | +/- |
| ▪ Palmitoylethanolamine (PEA) topically or PO | 5 | D | +/- |
| ▪ A-lipoic-acid (thioctic acid), amifostine, amitriptyline, acetyl-L-car-nitine, carbamazepine, electrolyte solutions, glutathione, Goshajinkigan (GJG), oxcarbazepine, vitamine B, vitamine E, or other compounds[1] | 1b | A | - |

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

Reviews/Leitlinien


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Nicht-medikamentöse Prävention

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*Kompression*

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*Kühlung*

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*Akupunktur*

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<u>Medikamentöse Prävention</u>

*Venlafaxin*

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*Palmitoylethanolamid (PEA)*

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*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.
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*Acetyl-L-Carnitin*

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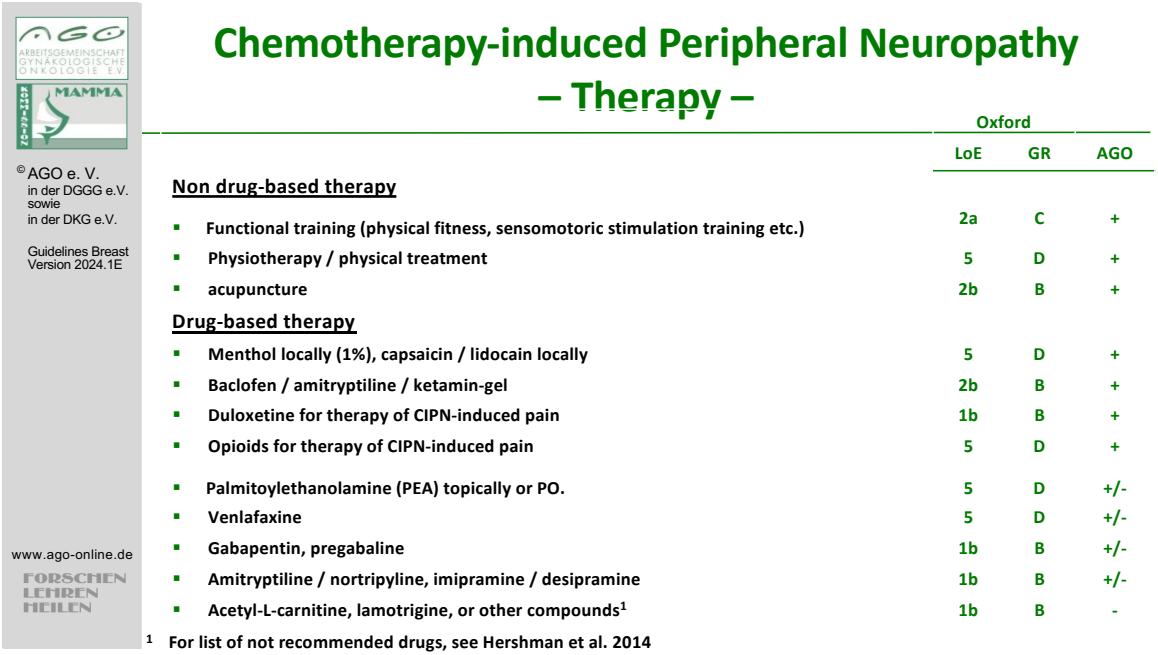


## Chemotherapy-induced Peripheral Neuropathy – Therapy –

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

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

Reviews / Leitlinien


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Nicht-medikamentöse Therapie

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*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
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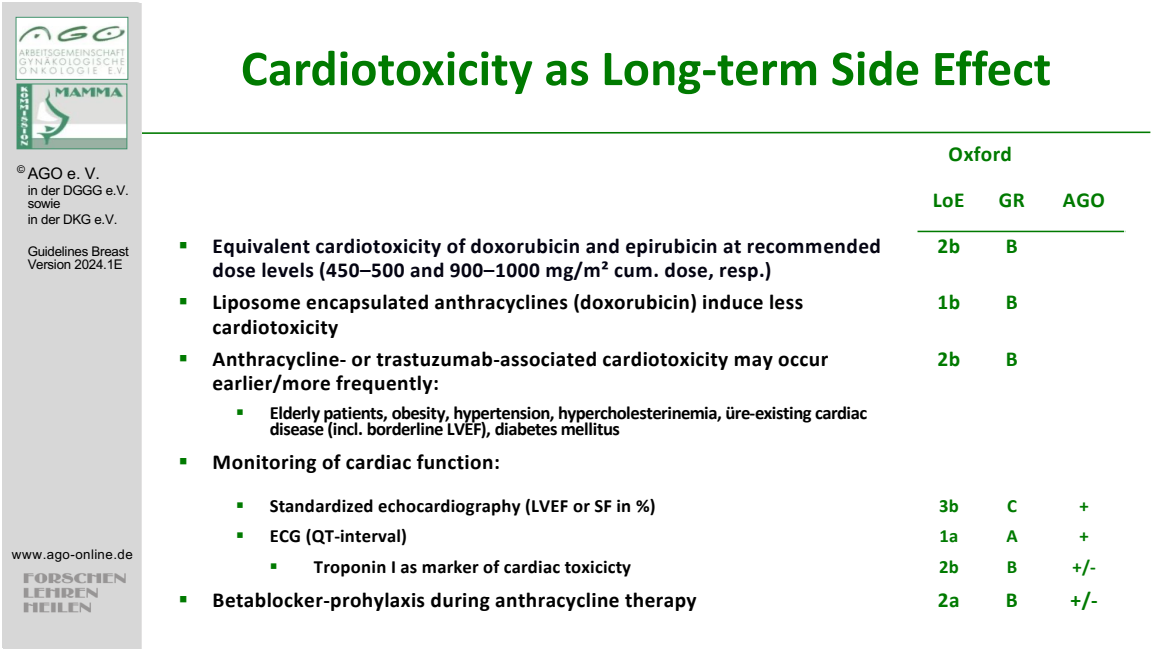
# 7. Cardiac Disorders

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Statements

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"Liposome encapsulated anthracyclines (doxorubicin) induce less cardiotoxicity"

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# Adjuvant Trastuzumab
# Cardiac Monitoring for CHF

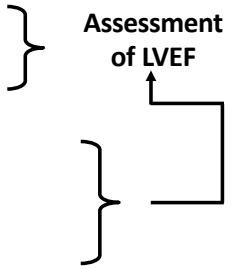
**Oxford LoE: 5** **GR: D** **AGO: ++**

**Before start of trastuzumab**
- History, physical examination (edema, hepatomegaly)
- Echocardiography (alternative to MUGA)

**During trastuzumab**
Regular assessment of
- Heart rate increase > 15% above individual base level
- Body weight increase ≥ 2 kg/week
- Cardiac signs and symptoms

**3 monthly assessment of LVEF**

**Assessment of LVEF**



Statement: Cardiac Monitoring (5 D ++)

Vote result of the AGO recommendation: 100%

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# Feasibility of Treatment Combinations Considering Toxicities

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| **Regarding cardiac toxicity** | | | |
| ▪ Trastuzumab simultaneous to radiotherapy | 2b | B | + |
| ▪ Trastuzumab simultaneous to epirubicin | 2b | B | +/- |
| ▪ Trastuzumab simultaneous to doxorubicin | 2b | B | - |
| ▪ Anthracycline simultaneous to radiotherapy | 2c | C | - |
| **Regarding lung and breast fibrosis** | | | |
| ▪ Tamoxifen simultaneous to radiotherapy | 3 | C | +/- |
| ▪ Chemotherapy simultaneous to radiotherapy | 1b | B | - |

Trastuzumab simultaneous to radiotherapy"

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"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]
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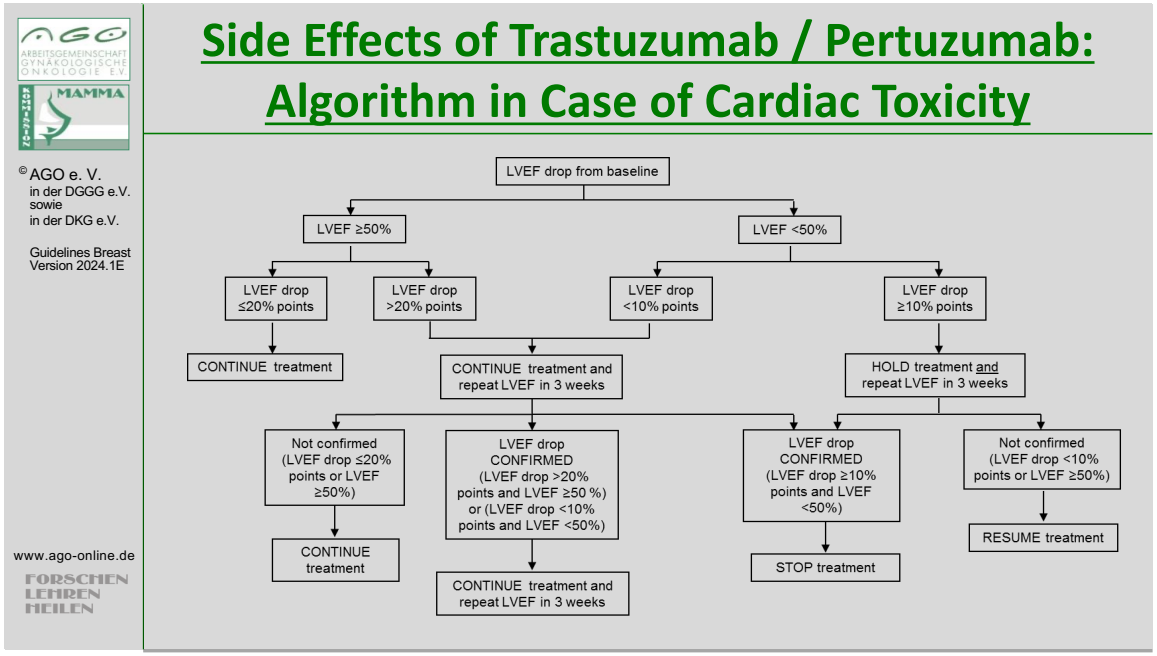



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# Side Effects According Organ Systems
## Incidence, Prevention, Therapy

## 8. Gastrointestinal Disorders

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

# Antiemetic Therapy

**http://www.mascc.org/antiemetic-guidelines**
**www.onkosupport.de**

| | Oxford LoE | Oxford GR | AGO |
|---|---|---|---|
| ▪ **After assessment of emetic potential of therapy protocol (p.o., i.v., s.c., i.m.)** | 5 | D | ++ |
| ▪ **Neurokinin-1-receptor-antagonists** | 1b | A | ++ |
| ▪ **Dexamethasone (also in chemotherapy combinations with ICPi)** | 1a | A | ++ |
| ▪ **5-$HT_3$-antagonists** | 1b | A | ++ |
| ▪ **Fixed antiemetic combination therapy** | 1b | A | ++ |
| ▪ **Rescue Medication** | | | |
| ▪ **Olanzapine** | 1b | A | + |
| ▪ **Levomepromazine, benzodiazepines** | 3b | C | + |
| ▪ **Cannabinoids, ginger** | 3b | C | +/- |

**ICPi = Immune Checkpoint inhibitor**

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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.
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Olanzapine

1 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.

2 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 2020;21:242-249.

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



Guidelines Breast
Version 2024.1E



## ACUTE Nausea and Vomiting: SUMMARY

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

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

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

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

Multinational Association of Supportive Care in Cancer
*Supportive Care Makes Excellent Cancer Care Possible*

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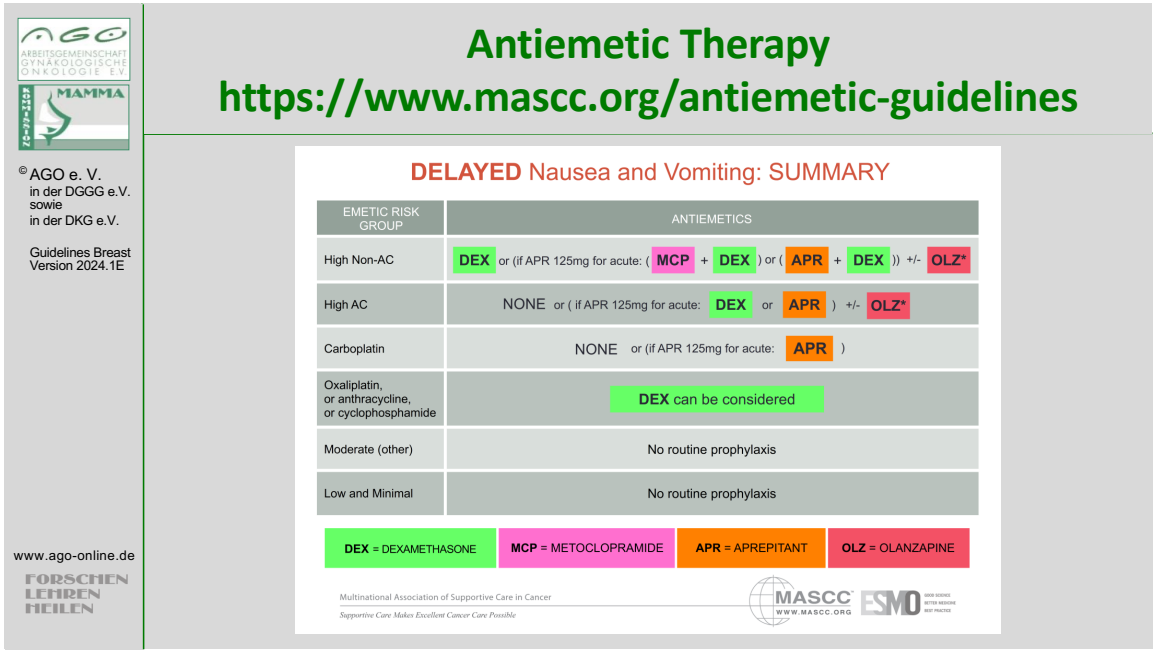


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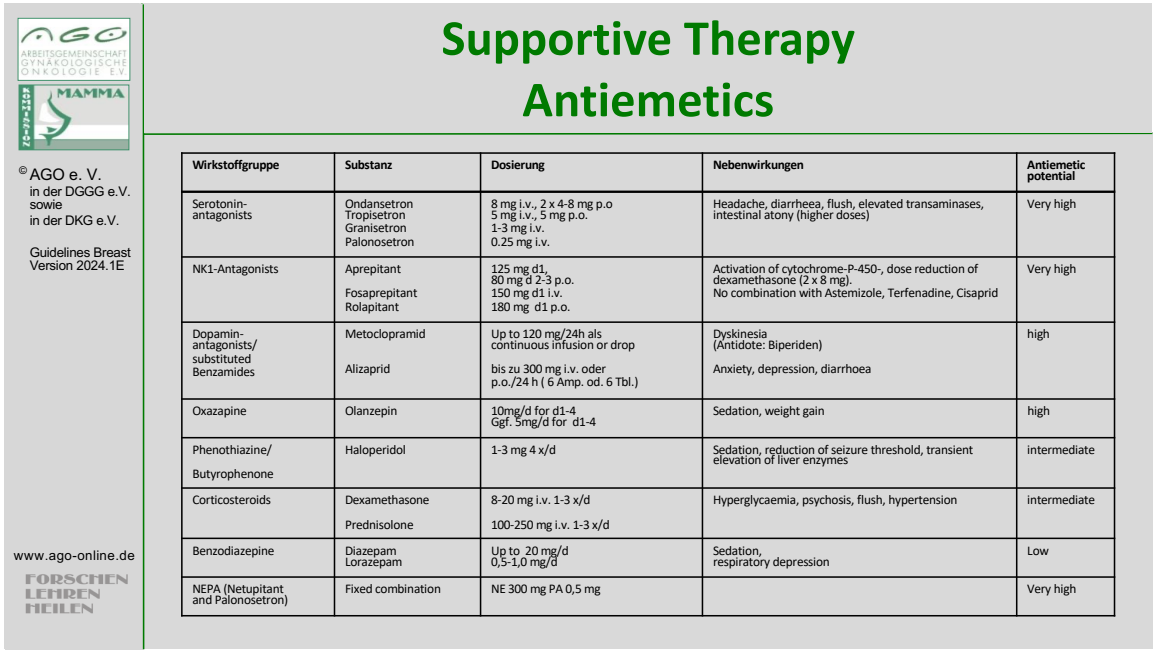


## Supportive Therapy
## Antiemetics

| Wirkstoffgruppe | Substanz | Dosierung | Nebenwirkungen | Antiemetic potential |
|---|---|---|---|---|
| Serotonin-antagonists | Ondansetron<br>Tropisetron<br>Granisetron<br>Palonosetron | 8 mg i.v., 2 x 4-8 mg p.o<br>5 mg i.v., 5 mg p.o.<br>1-3 mg i.v.<br>0.25 mg i.v. | Headache, diarrheea, flush, elevated transaminases, intestinal atony (higher doses) | Very high |
| NK1-Antagonists | Aprepitant<br>Fosaprepitant<br>Rolapitant | 125 mg d1,<br>80 mg d 2-3 p.o.<br>150 mg d1 i.v.<br>180 mg d1 p.o. | Activation of cytochrome-P-450-, dose reduction of dexamethasone (2 x 8 mg).<br>No combination with Astemizole, Terfenadine, Cisaprid | Very high |
| Dopamin-antagonists/ substituted Benzamides | Metoclopramid<br>Alizaprid | Up to 120 mg/24h als continuous infusion or drop<br>bis zu 300 mg i.v. oder p.o./24 h ( 6 Amp. od. 6 Tbl.) | Dyskinesia (Antidote: Biperiden)<br>Anxiety, depression, diarrhoea | high |
| Oxazapine | Olanzepin | 10mg/d for d1-4<br>Ggf. 5mg/d for d1-4 | Sedation, weight gain | high |
| Phenothiazine/<br>Butyrophenone | Haloperidol | 1-3 mg 4 x/d | Sedation, reduction of seizure threshold, transient elevation of liver enzymes | intermediate |
| Corticosteroids | Dexamethasone<br>Prednisolone | 8-20 mg i.v. 1-3 x/d<br>100-250 mg i.v. 1-3 x/d | Hyperglycaemia, psychosis, flush, hypertension | intermediate |
| Benzodiazepine | Diazepam<br>Lorazepam | Up to 20 mg/d<br>0,5-1,0 mg/d | Sedation,<br>respiratory depression | Low |
| NEPA (Netupitant and Palonosetron) | Fixed combination | NE 300 mg PA 0,5 mg | | Very high |

Olanzapine


1. 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.
2. 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 2020;21:242-249.
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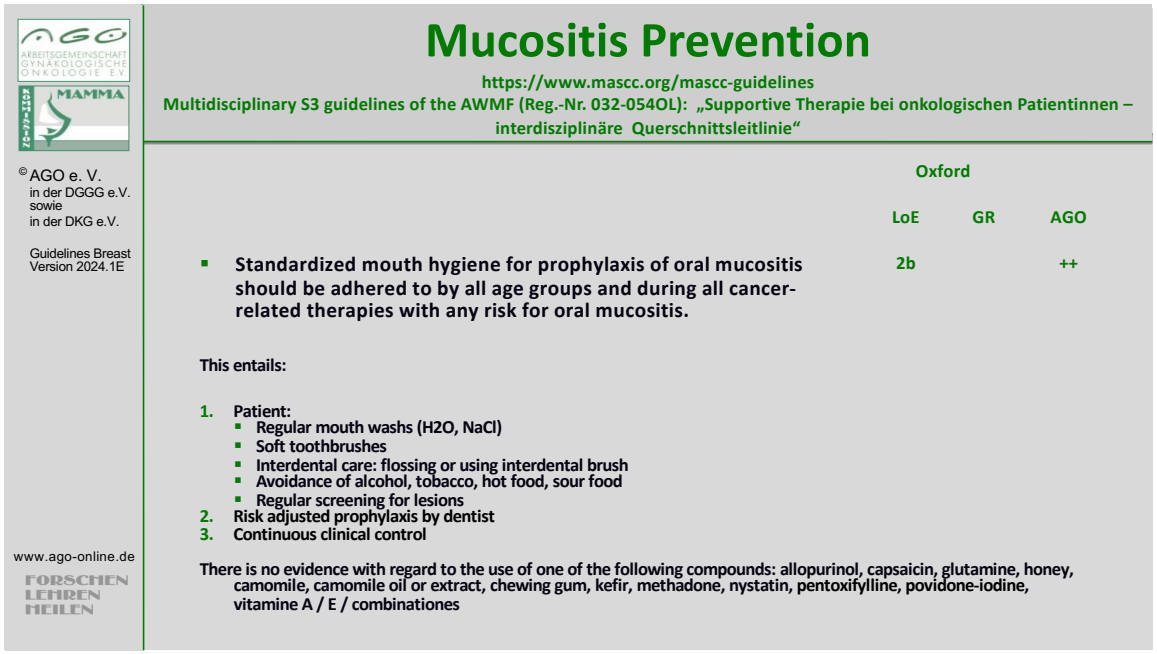



Relevant practice guideline

Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3, Februar 2020, AWMF Registernummer: 032/054OL, http://leitlinienprogramm-onkologie.de/Supportive-Therapie.95.0.html (Zugriff am 27.12.2021)

1. Elad S, Fong Cheng KK, Lalla RV, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. Cancer 2020;126:4423-4431.
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.
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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.
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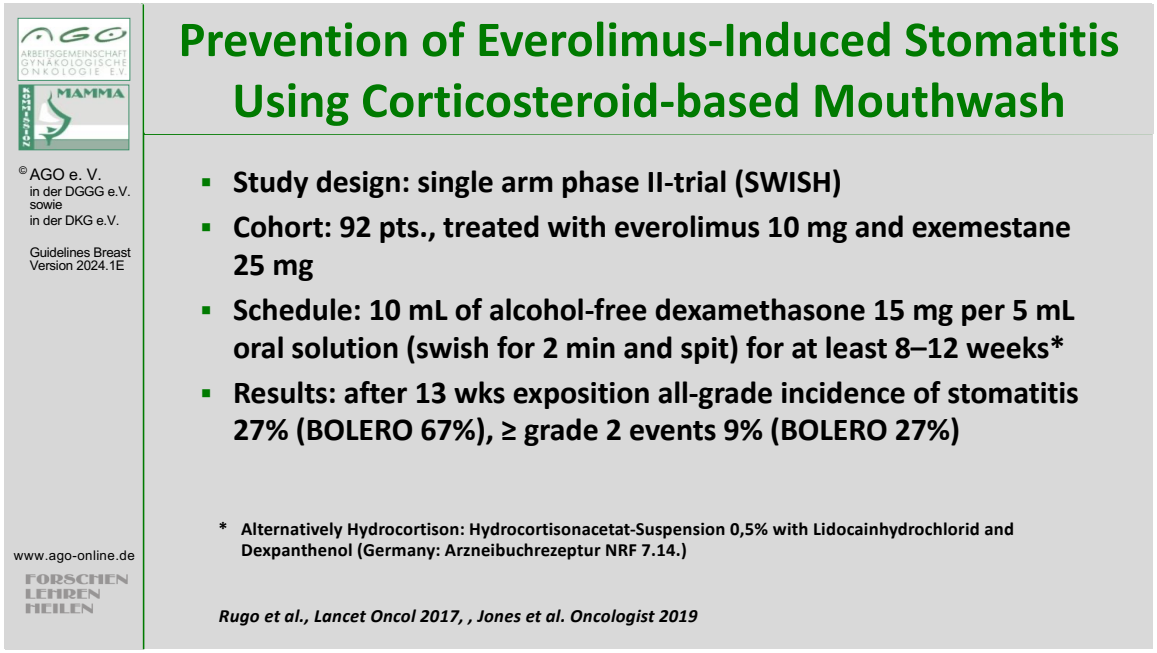



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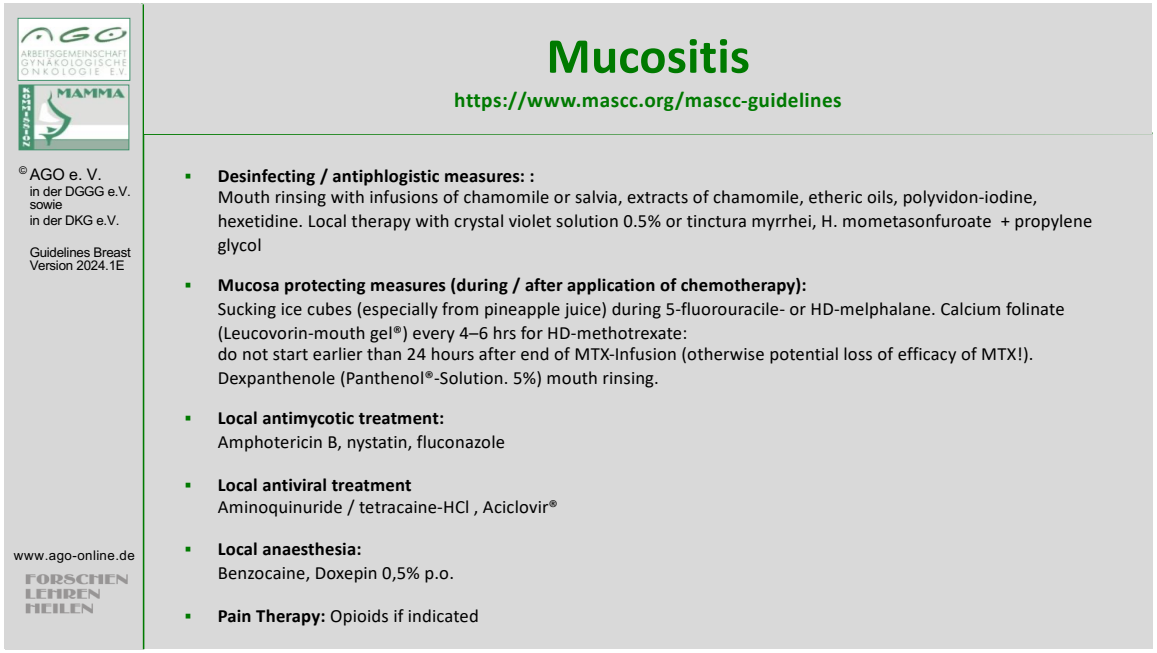


<u>Relevant practice guideline</u>

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4. 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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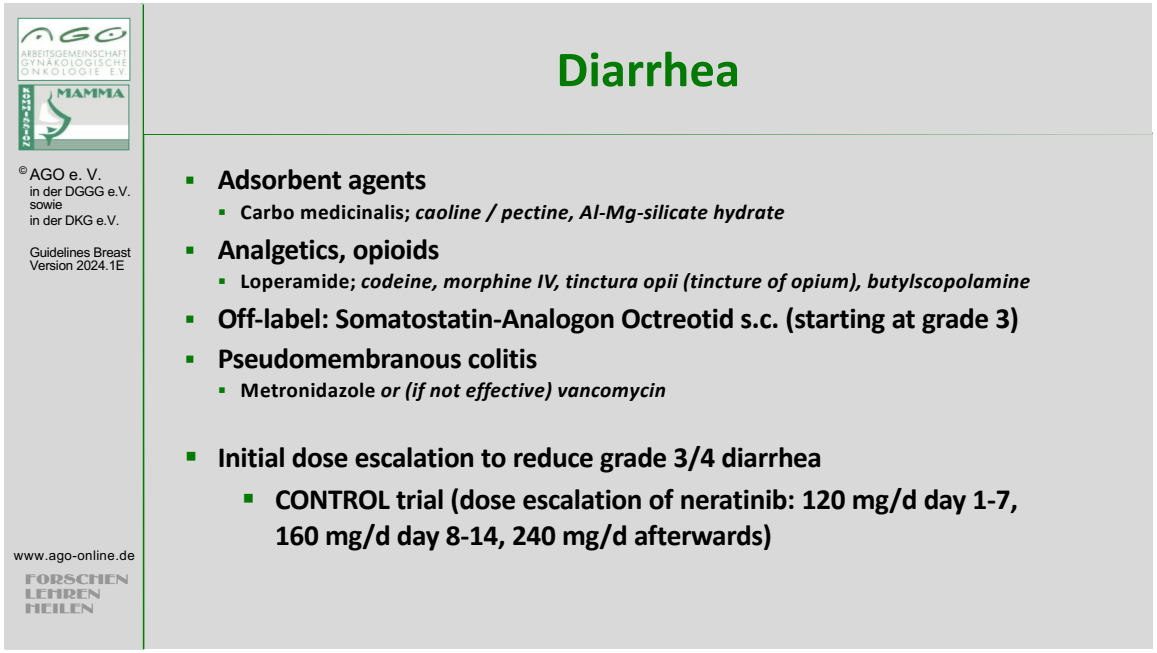



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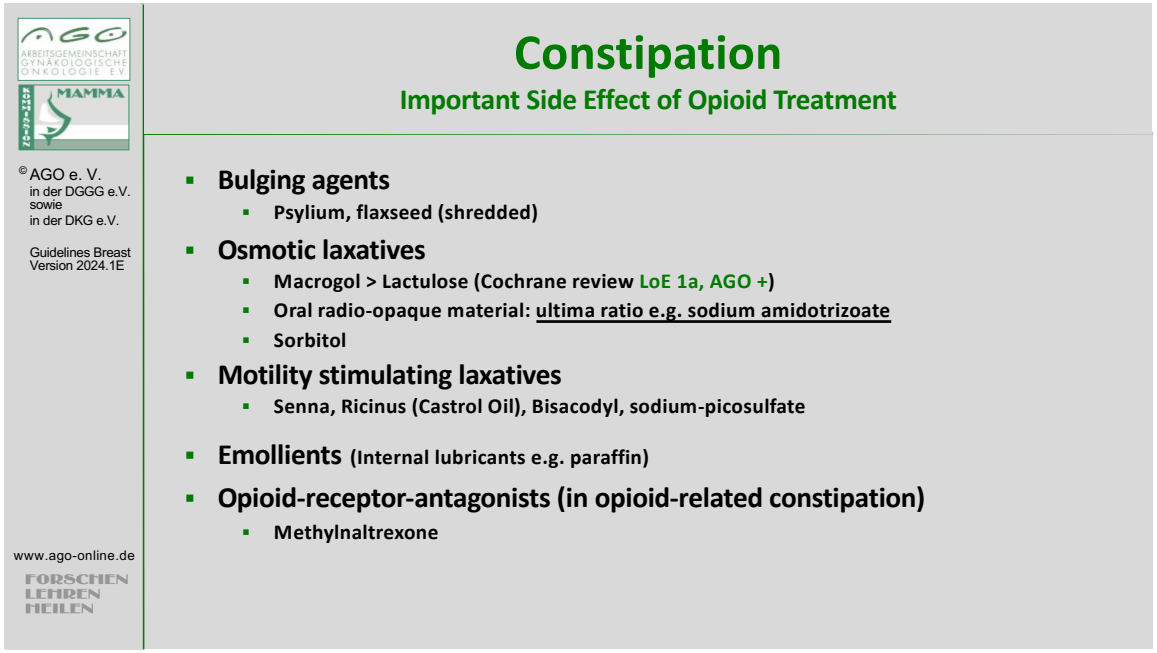


Relevant practice guideline

1. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3, Februar 2020, AWMF Registernummer: 032/054OL, http://leitlinienprogramm-onkologie.de/Supportive-Therapie.95.0.html (Zugriff am 27.12.2021)

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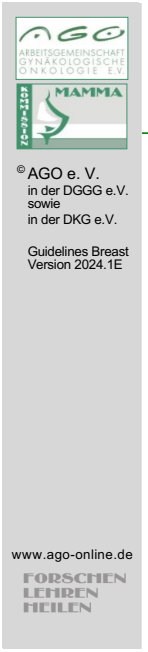
# 9. Skin & Subcutaneous Tissue Disorders (Alopecia)

Relevant practice guideline

1. 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)




# Skin Toxicities

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ Avoidance of chemotherapy-induced alopecia by cooling the patient's scalp* | 1b | | +/- |
| ▪ Prophylaxis of hand-foot-syndrome using urea containing lotions (5-10%) | 1b | | + |
| ▪ Prophylaxis of nail changes and hand-foot-syndrome by cooling hands during application of docetaxel | 2b | | + |

* Substance- and regimen specific


Relevant practice guidelines

1. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3, Februar 2020, AWMF Registernummer: 032/054OL, http://leitlinienprogramm-onkologie.de/Supportive-Therapie.95.0.html (Zugriff am 27.12.2021)
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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.
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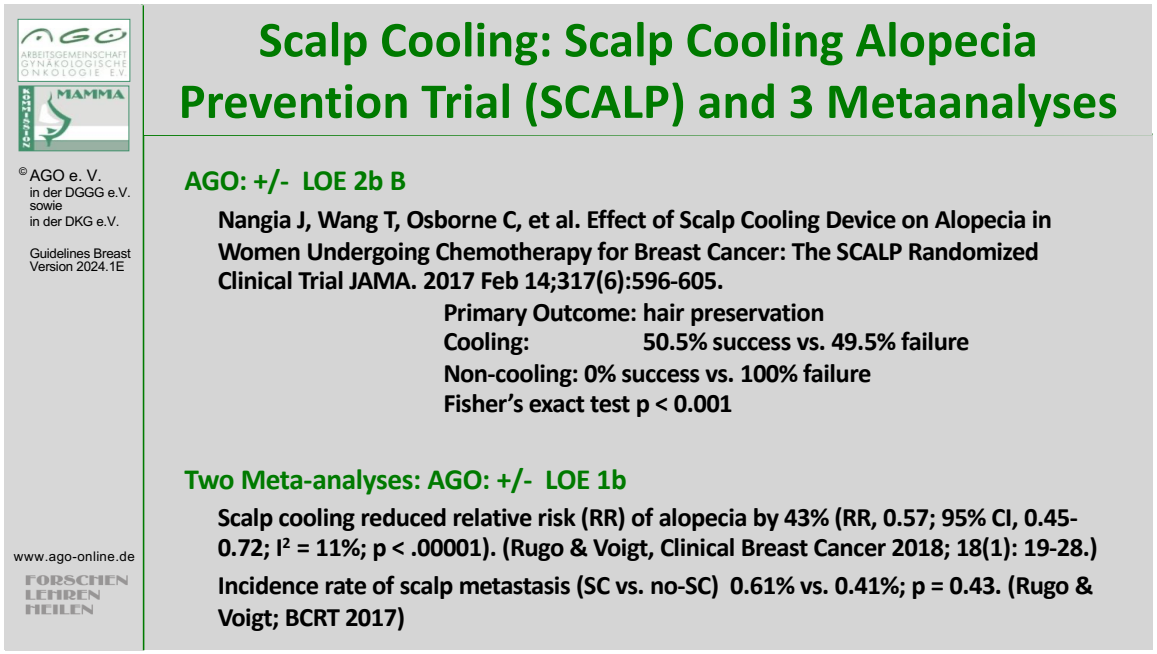



1. Nangia J, Wang T, Osborne C, et al. Effect of Scalp Cooling Device on Alopecia in Women Undergoing Chemotherapy for Breast Cancer: The SCALP Randomized Clinical Trial JAMA. 2017 Feb 14;317(6):596-605.
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# 10. Musculoskeletal & connective tissue disorders

***(see Chapter Osteooncology)***

Relevant practice guideline

1. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3, Februar 2020, AWMF Registernummer: 032/054OL, http://leitlinienprogramm-onkologie.de/Supportive-Therapie.95.0.html (Zugriff am 27.12.2021)

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# 11. General Disorders & Administration Site Conditions

Relevant practice guideline

1. 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)

# Extravasation of Potentially Necrotizing Compounds (Anthracyclines, Taxanes, Vinorelbine)

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| ▪ **Dexrazoxane for treatment of anthracycline-extravasations (exception: liposomal Anthracyclines)** | 2b | B | ++ |
| ▪ **Hyaluronic acid for treatment of taxane / vinorelbine-extravasations (off-label use)** | 3b | B | + |

Relevant practice guideline:

1. Hensley ML, Hagerty KL, Kewalramani T et al. American Society of Clinical Oncology 2008 clinical practice guideline update: use of chemotherapy and radiation therapy protectants. J Clin Oncol. 2009 Jan 1;27(1):127-45.
2. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3, 2020, AWMF Registernummer: 032/054OL

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.
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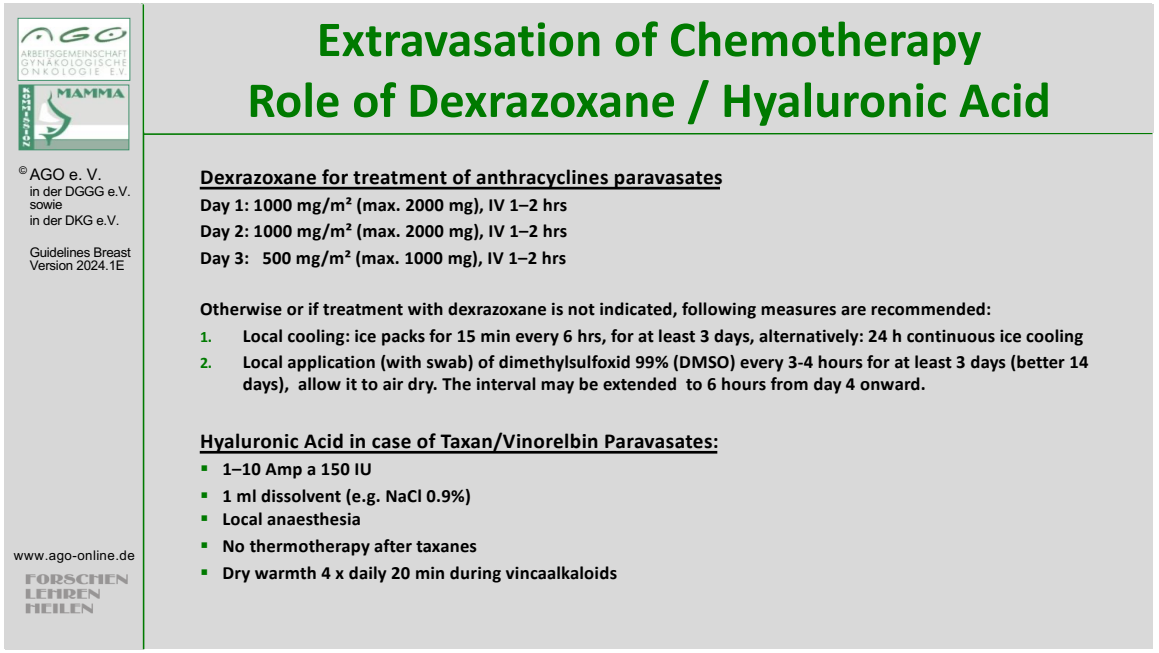
Hyaluronsäure

siehe S3-Leitlinie, Kapitel 11: Paravasate.




Relevant practice guideline

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# 11. Lung

Relevant practice guideline

1. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3, 2020, AWMF Registernummer: 032/054OL, http://leitlinienprogramm- onkologie.de/Supportive-Therapie.95.0.html (Zugriff am 17.01.2022)

# Drug-induced Pneumonitis, Interstitial Lung Disease (ILD)

| | Oxford | | |
|---|---|---|---|
| | LoE | GR | AGO |
| **Diagnostic work-up with chest CT** | 1a | B | ++ |
| **Therapy according to grade and drug*** | | | |
| **Corticosteroids (start with ≥ 0.5 mg/kg/d prednisolone-equivalent)** | 1a | B | ++ |
| **Dose hold or therapy discontinuation* (according to respective product information)** | 1b | B | ++ |

1. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.3, 2020, AWMF Registernummer: 032/054OL
2. Skeoch S, Weatherley N, Swift AJ, et al. Drug-Induced Interstitial Lung Disease: A Systematic Review. J Clin Med. 2018 Oct 15;7(10):356.
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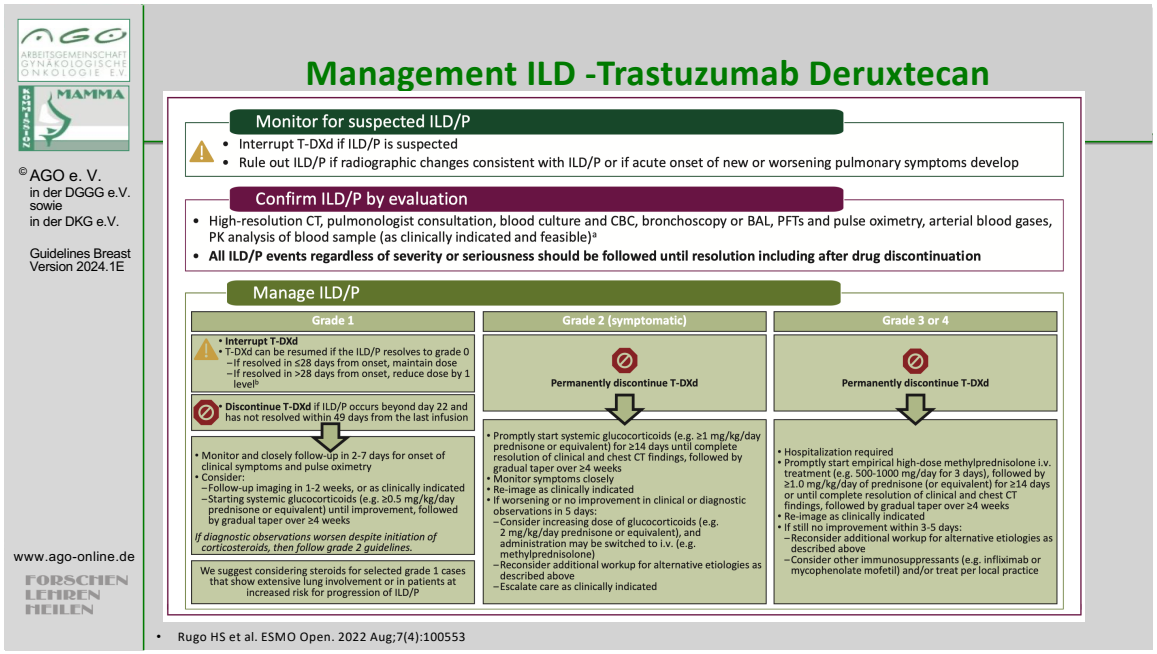



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# Further Supportive and Palliative Issues

- **Orphan symptome (from ESMO-guideline for orphan symptoms 2020):**
  - **Muscle cramps**
  - **Myoclonus**
  - **Taste alterations**
  - **Dry mouth (Xerostomia)**
  - **Cough, Hiccup**
  - **Rectal tenesmus**
  - **Restless legs-syndrom**

- **Further issues**
  - **Nutrition**
  - **Pain management**
  - **Palliative Care**
  - **CNS metastases (see chapter)**

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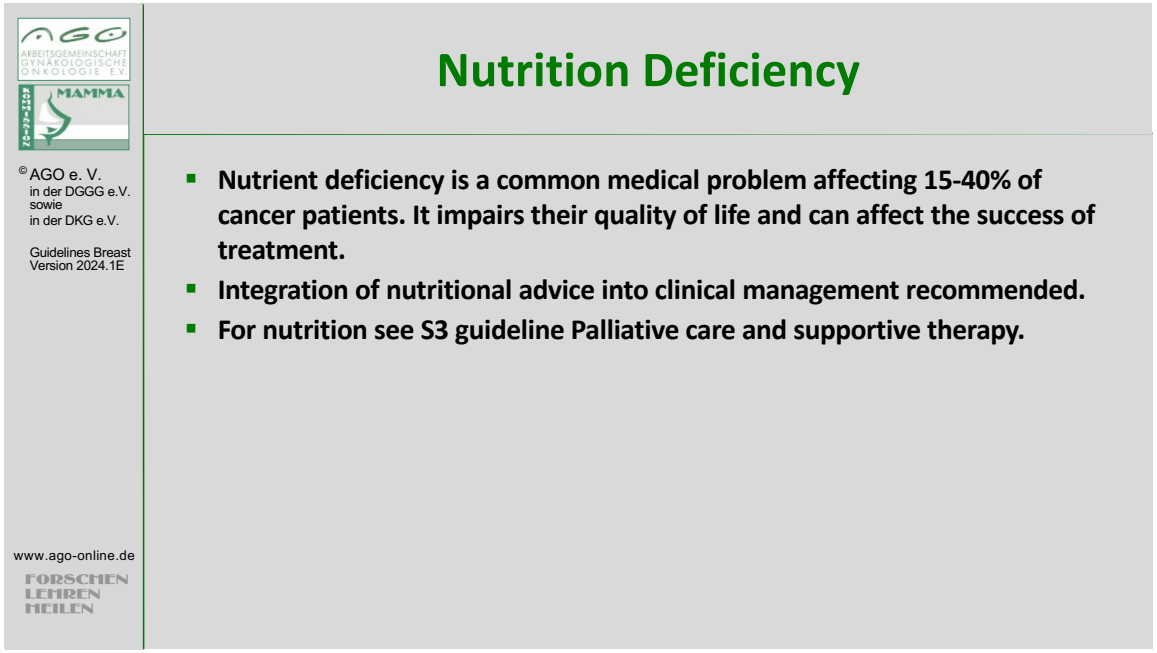



Klinische Ernährung

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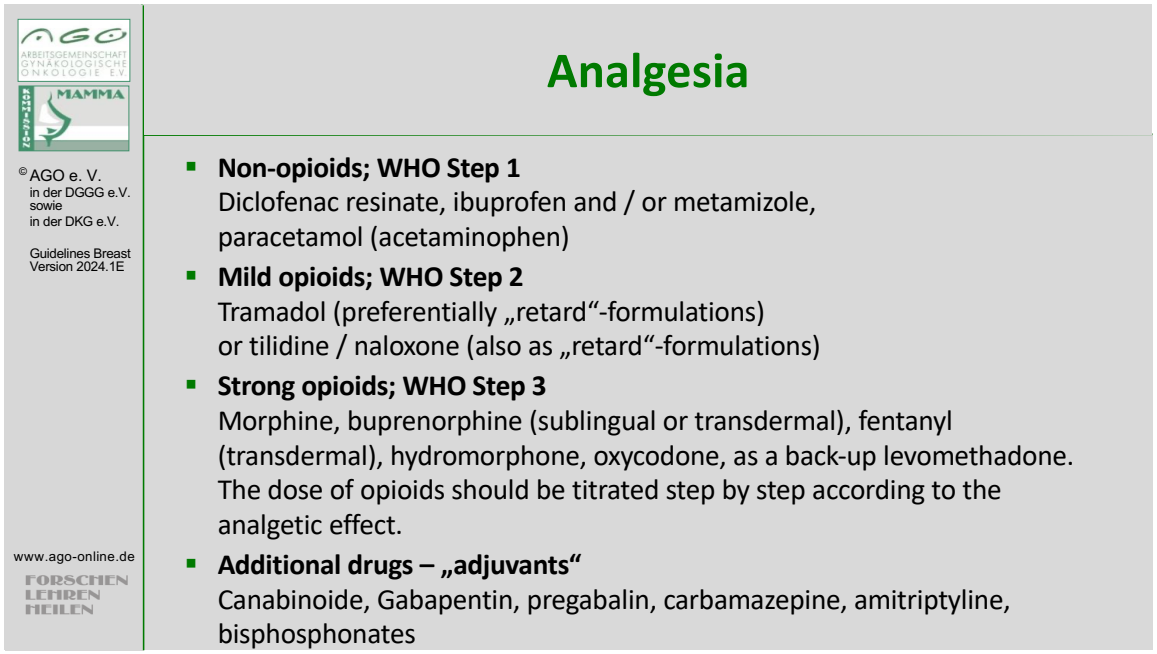


Relevant practice guideline:


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3. Horlemann J, Schürmann N. DGS Praxisleitlinien in der Schmerztherapie. Cannabis in der Schmerzmedizin v1.0. https://dgs-praxisleitlinien.de/cannabis/ (Zugriff 27.12.2021)


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