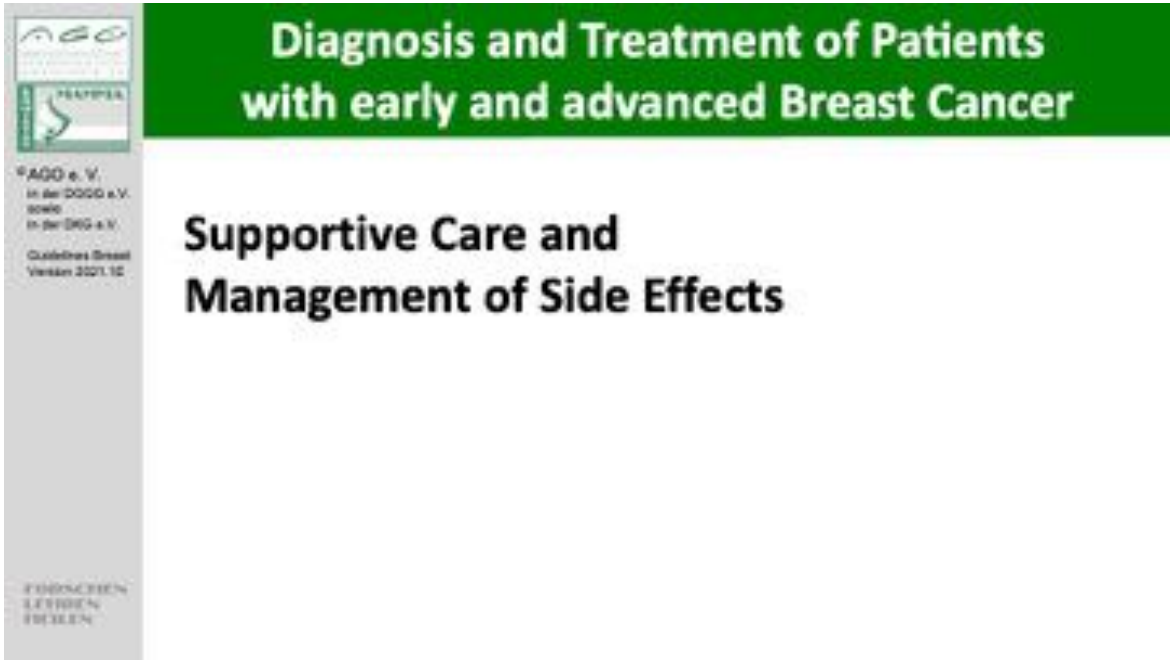

Screened data bases

Pubmed 2007 - 2020, ASCO 2010 – 2020, SABCS 2010 – 2020, 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.
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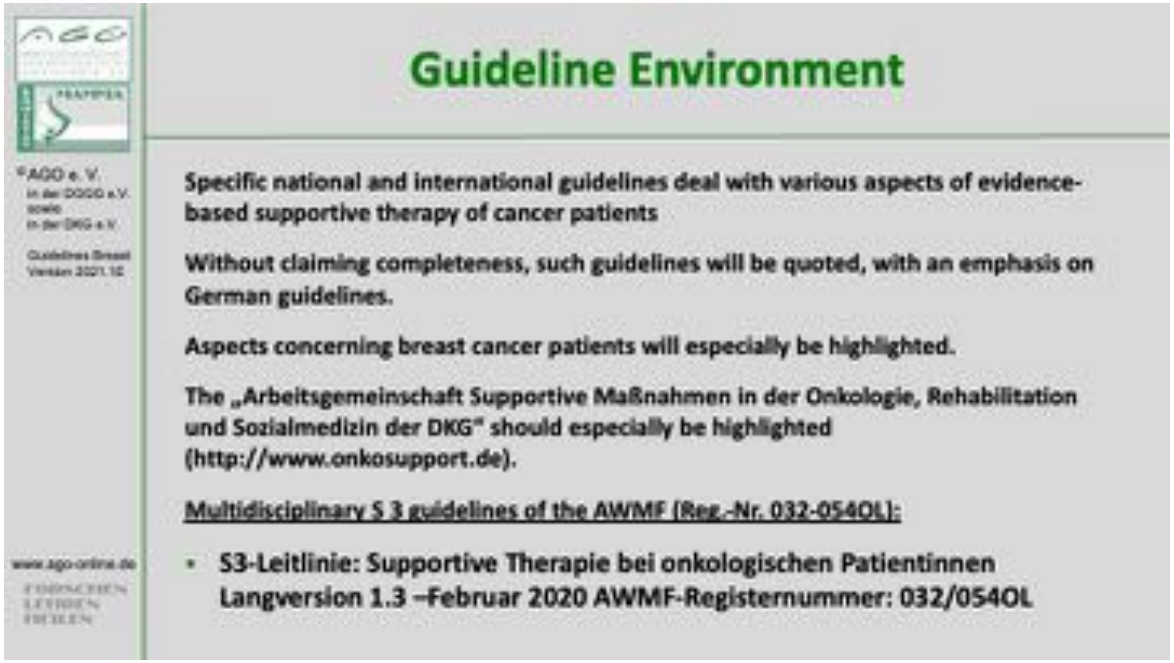
8. S3-Leitlinie: Supportive Therapie:
Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Supportive Therapie bei onkologischen PatientInnen - Langversion 1.2 – November 2019 AWMF-Registernummer: 032/054OL Zugrifff 26.12.2019

Supportive Care and Management of Side Effects

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

- **Version 2021:**
  Mundhenke/Nitz

- **Guideline - environment**



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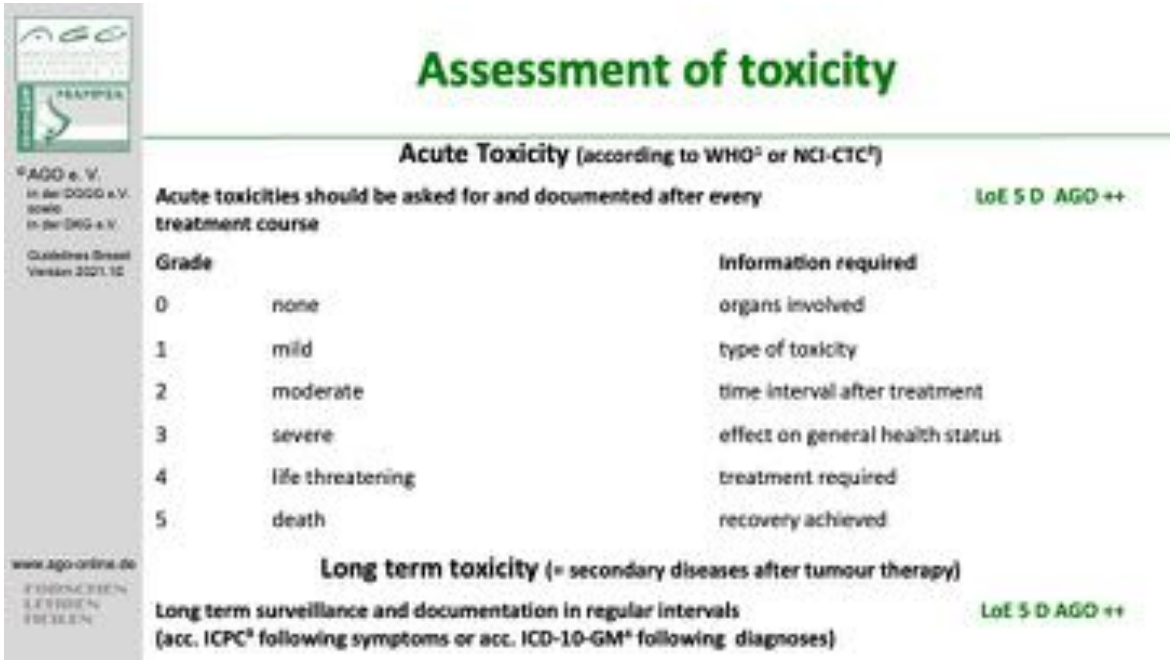
- **Assessment of toxicity**
  - **Acute toxicity (NCI-CTCAE)**
  - **Long-term toxicity (ICPC, ICD-GM)**



Assessment of toxicity

Acute Toxicity (according to WHO[2] or NCI-CTC[3])

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 (acc. ICPC[8] following symptoms or acc. ICD-10-GM[4] following diagnoses) — LoE 5 D AGO ++

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.
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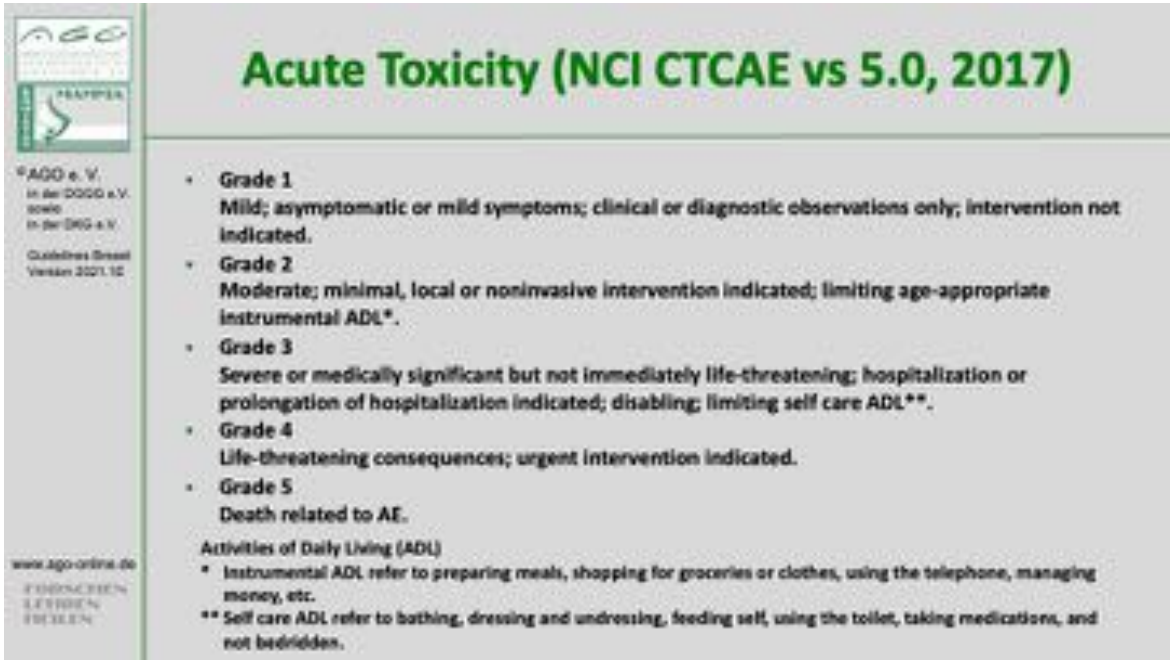
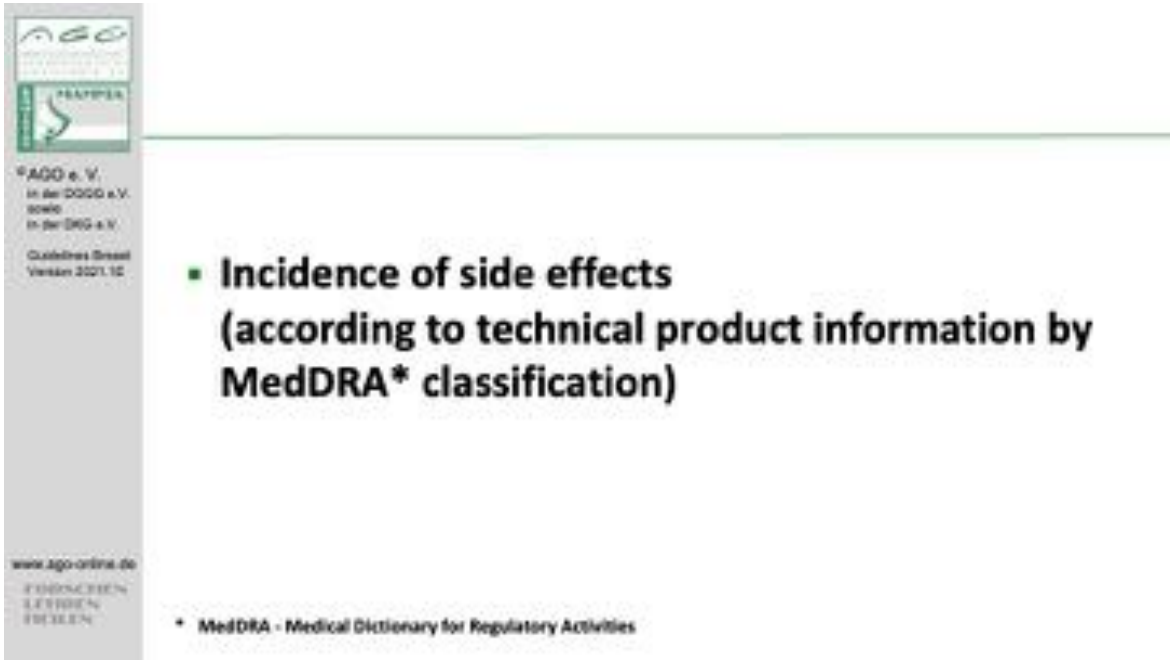
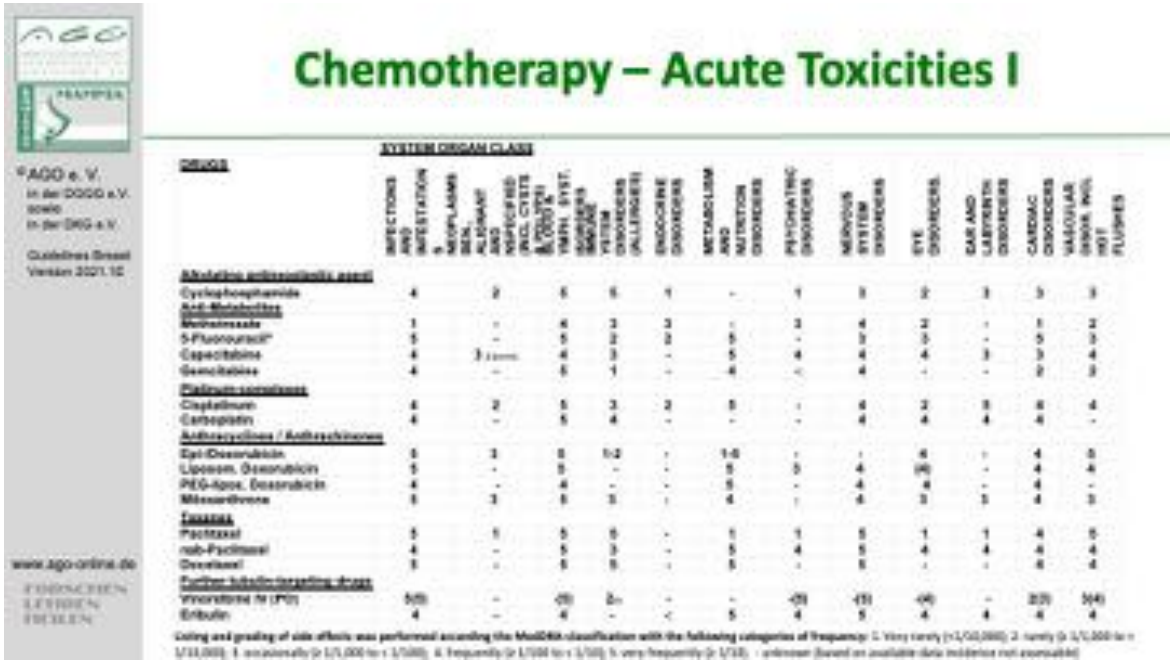


1. NCI, Bethesda, USA, Common Terminology Criteria for Adverse Events v5.0 (CTCAE; published 2017); https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50 (Download 18.01.2018)



*MedDRA - Medical Dictionary for Regulatory Activities
https://www.meddra.org/



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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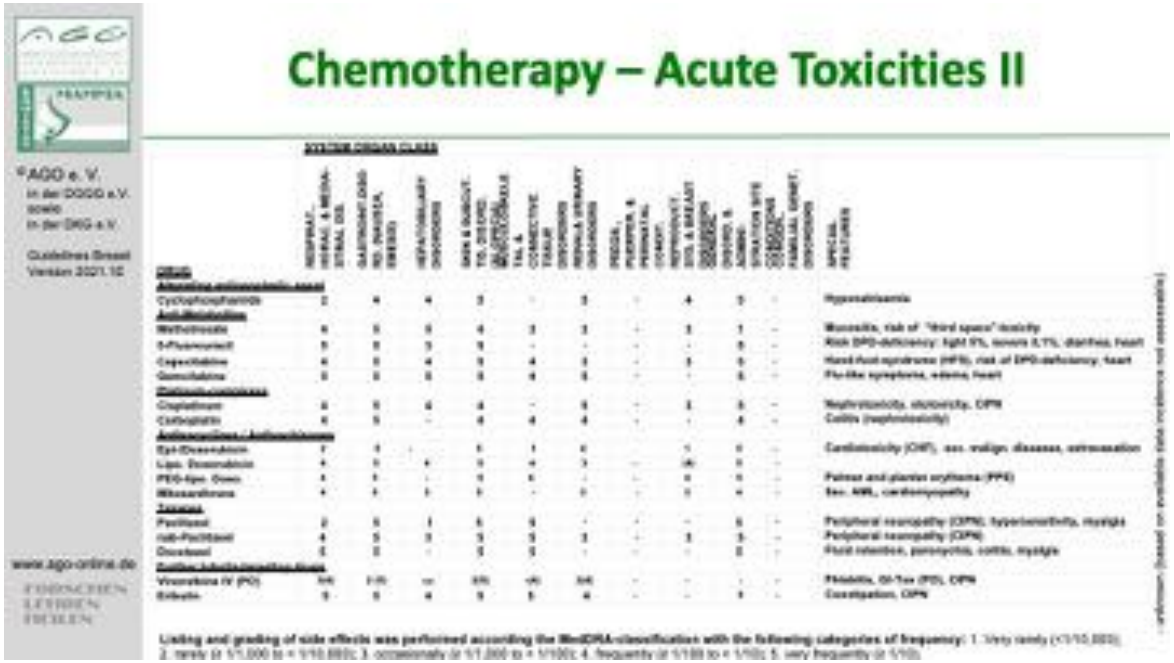
10. Crawford J.
11. NCCN, editor. NCCNR Practice Guidelines in Oncology - v.1.2011; Myeloid Growth Factors. National Comprehensive Cancer Network 2011. 18-7-2011.
12. Madeddu C, Deidda M, Piras A, et al. Pathophysiology of cardiotoxicity induced by nonanthracycline chemotherapy. J Cardiovasc Med (Hagerstown). 2016 May;17 Suppl 1 Special issue on Cardiotoxicity from Antiblastic Drugs and Cardioprotection:e12-e18. Review.



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

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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

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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
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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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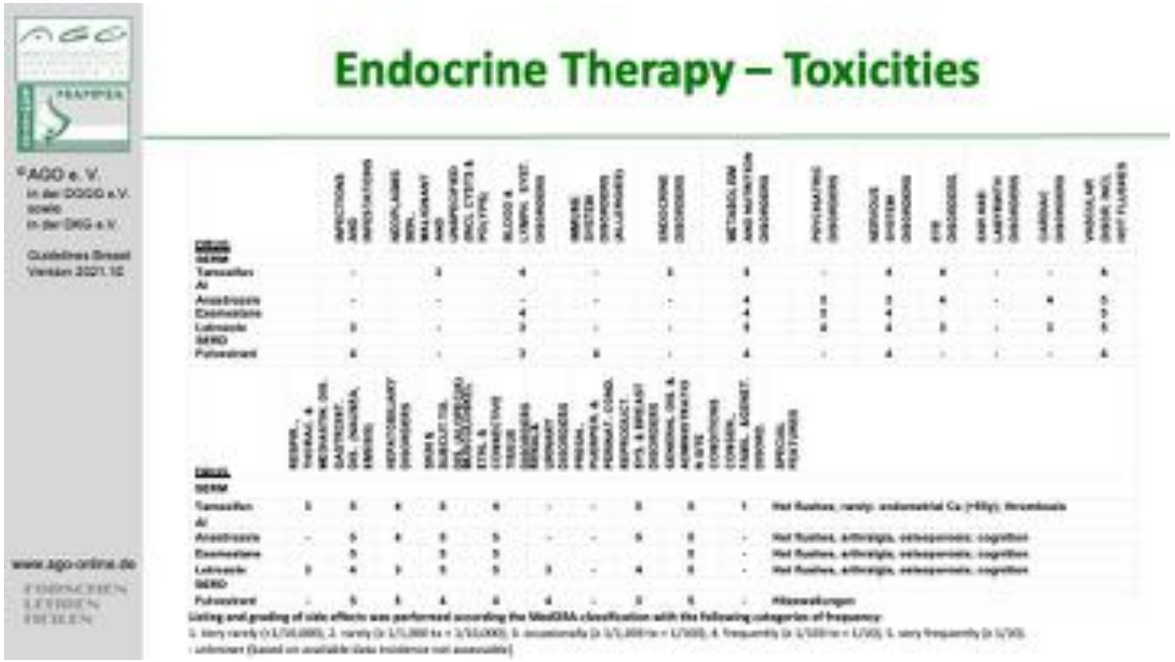

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Tamoxifen: https://www.gelbe-liste.de/produkte/Tamoxifen-20-mg-HEXAL-Filmtbl_8660/fachinformation
Anastrozol: https://imedikament.de/anastrozol-ratiopharm-1-mg-filmtabletten/fachinformation
Exemestan: http://www.success-studie.de/c/downloads/Fachinfo/FI_ExemestanAromasin.pdf
Letrozol: http://www.success-studie.de/b/downloads/Fachinfo/Femara_Juli_2014.pdf
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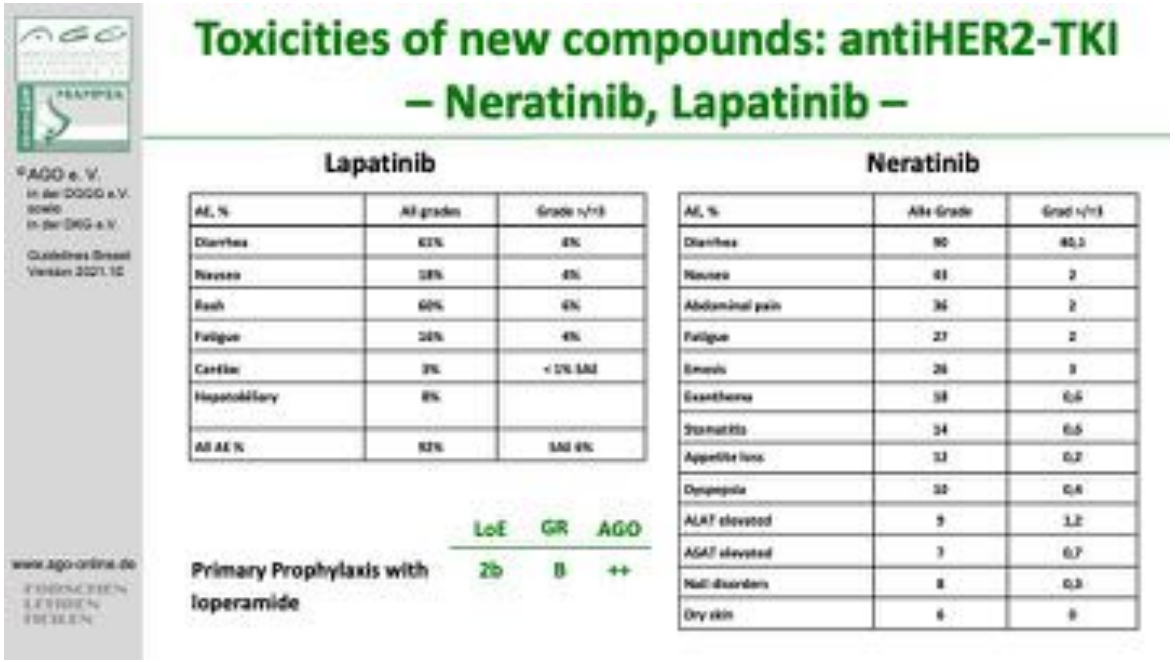

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Common Toxicities with antiHER2-TKI: Tucatinib, Trastuzumab + Capecitabine

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

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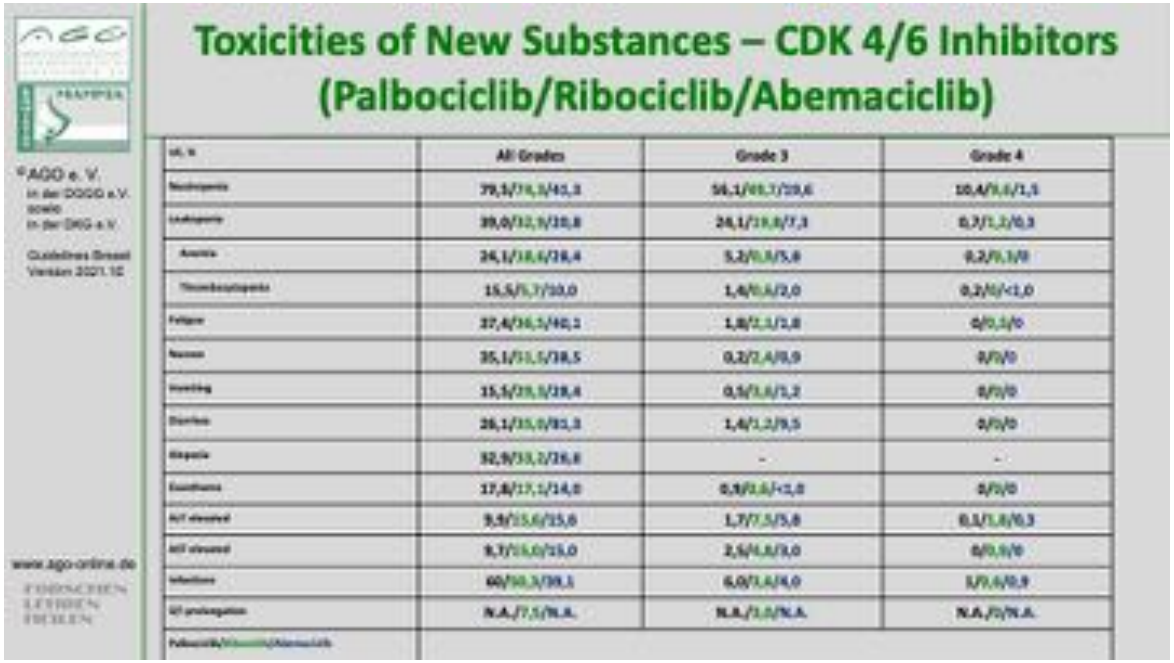

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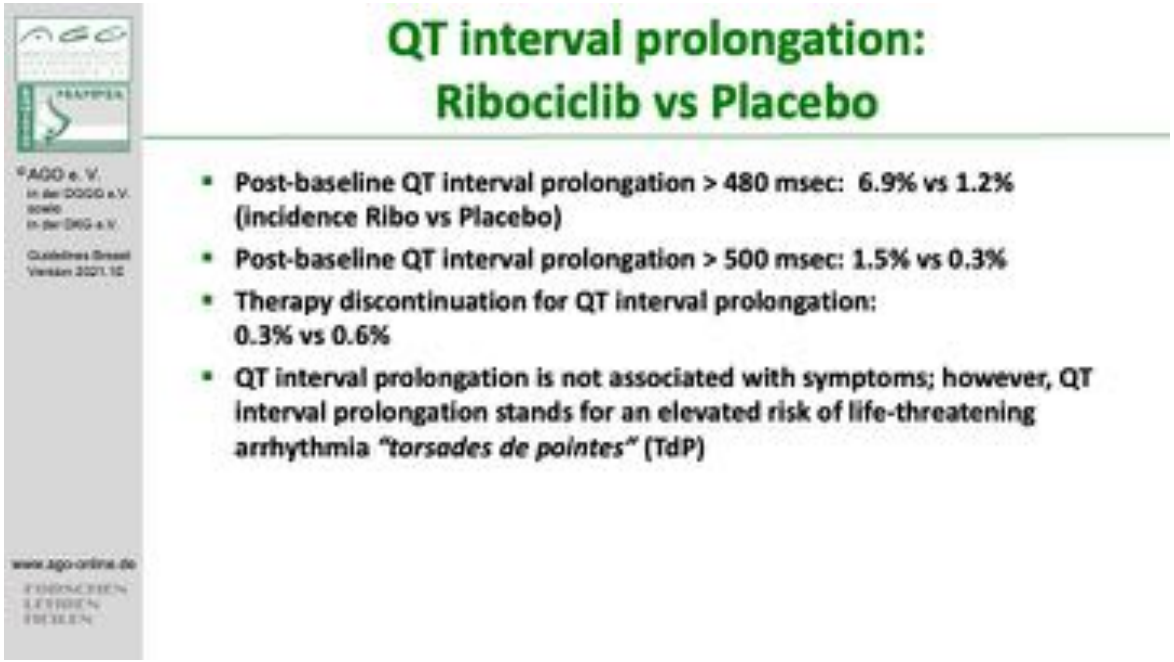

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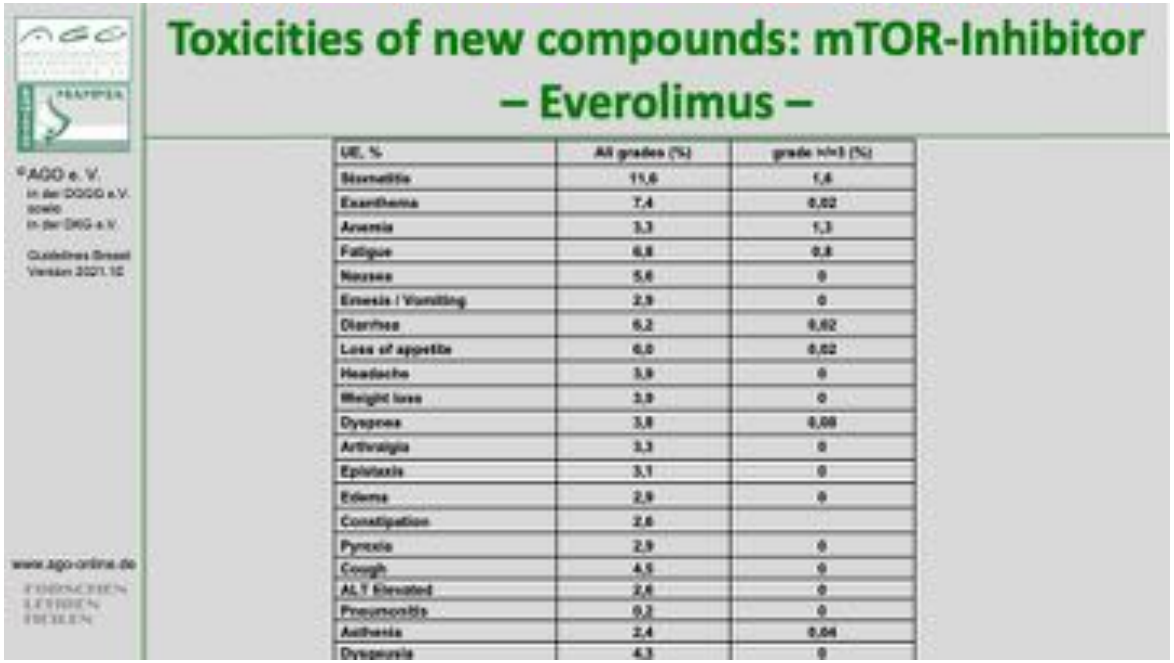

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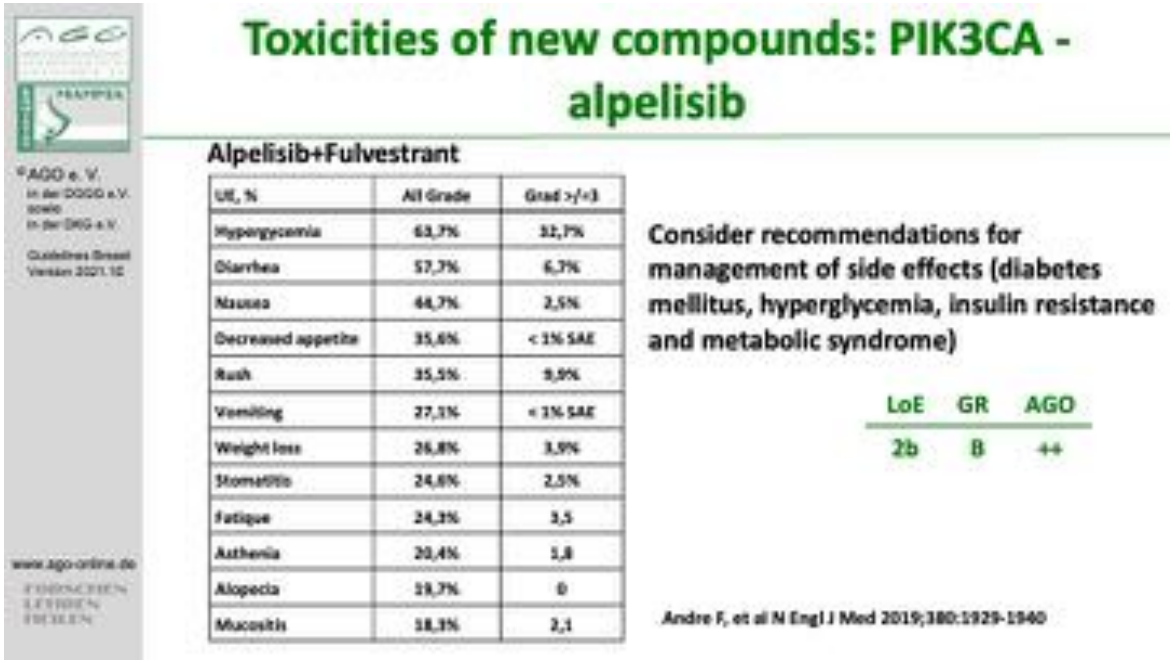

UE, %	All Grade	Grad >/=3
Hyperglycemia	63,7%	32,7%
Diarrhea	57,7%	6,7%
Nausea	44,7%	2,5%
Decreased appetite	35,6%	< 1% SAE
Rash	35,5%	9,9%
Vomiting	27,1%	< 1% SAE
Weight loss	26,8%	3,9%
Stomatitis	24,6%	2,5%
Fatigue	24,3%	3,5
Asthenia	20,4%	1,8
Alopecia	19,7%	0
Mucositis	18,3%	2,1

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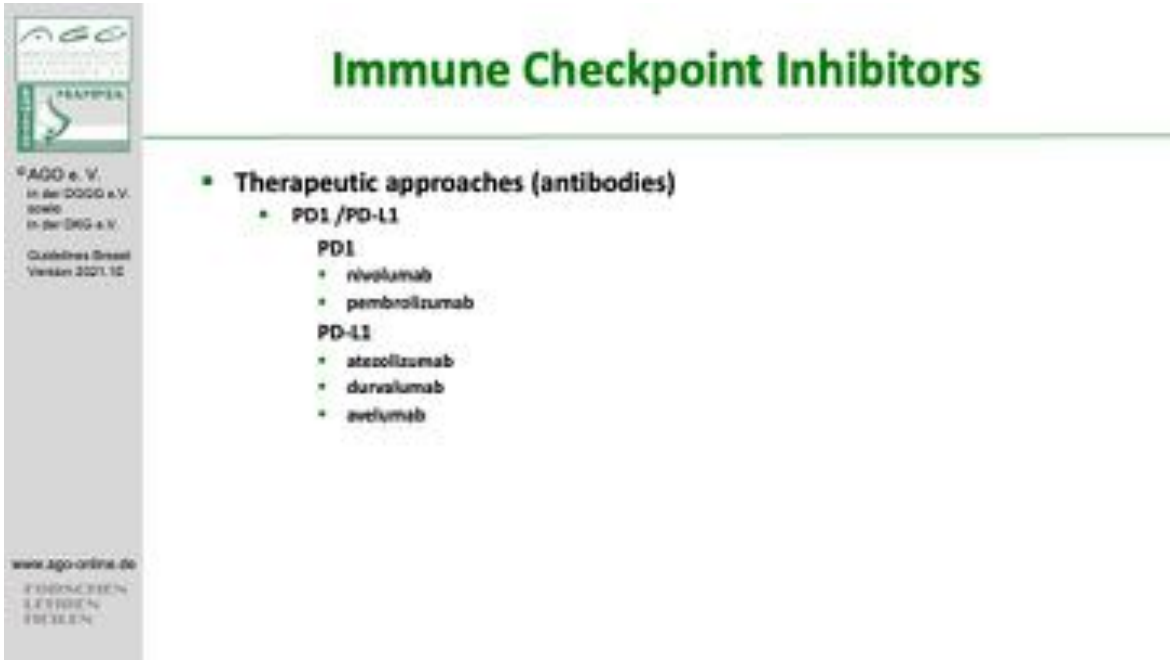

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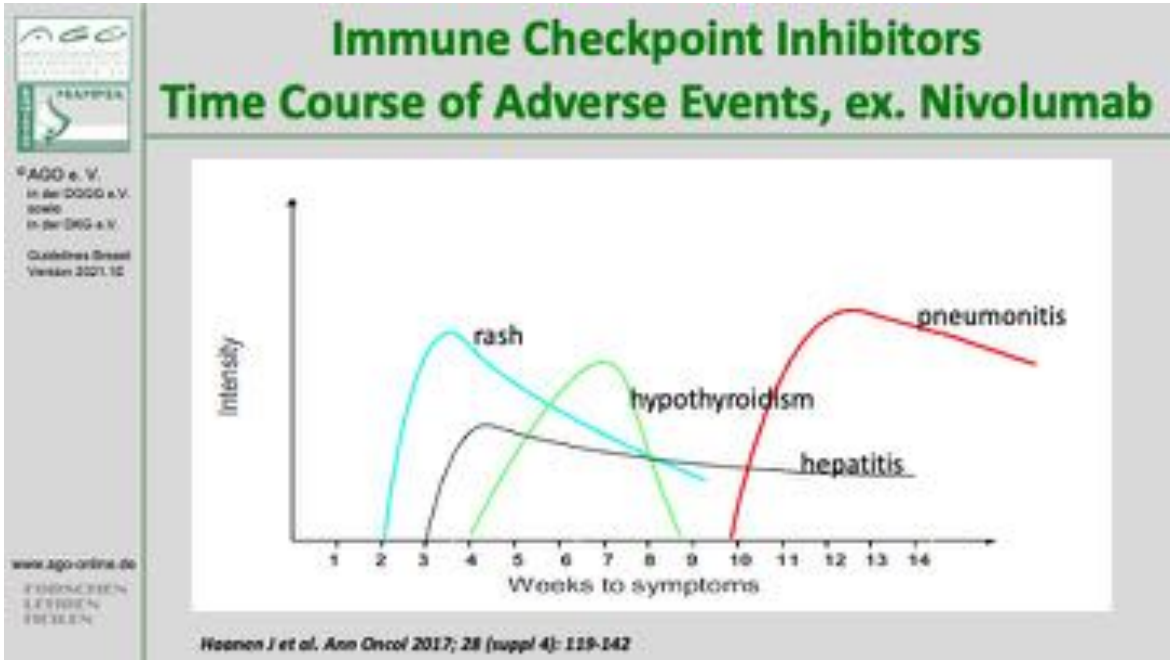

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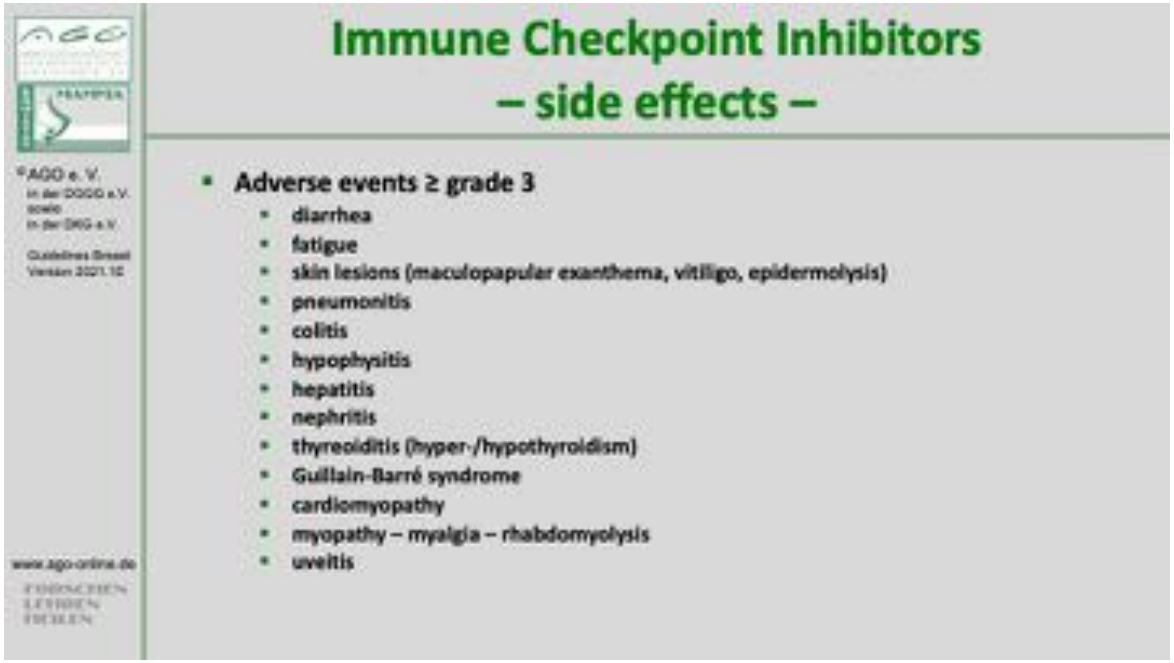

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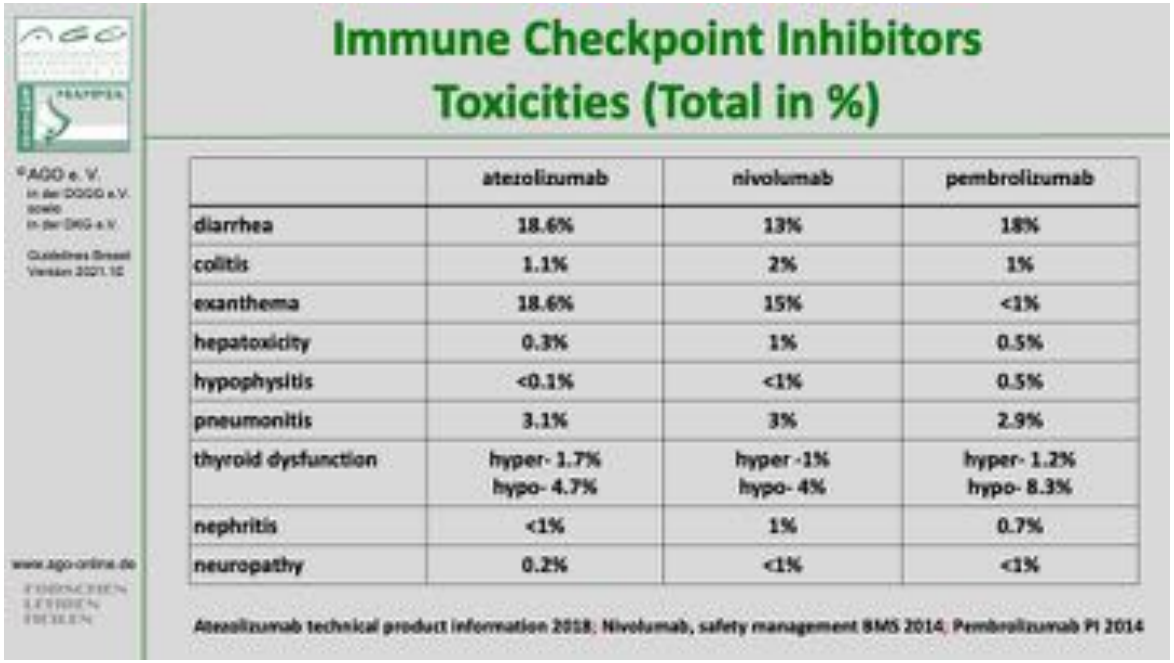
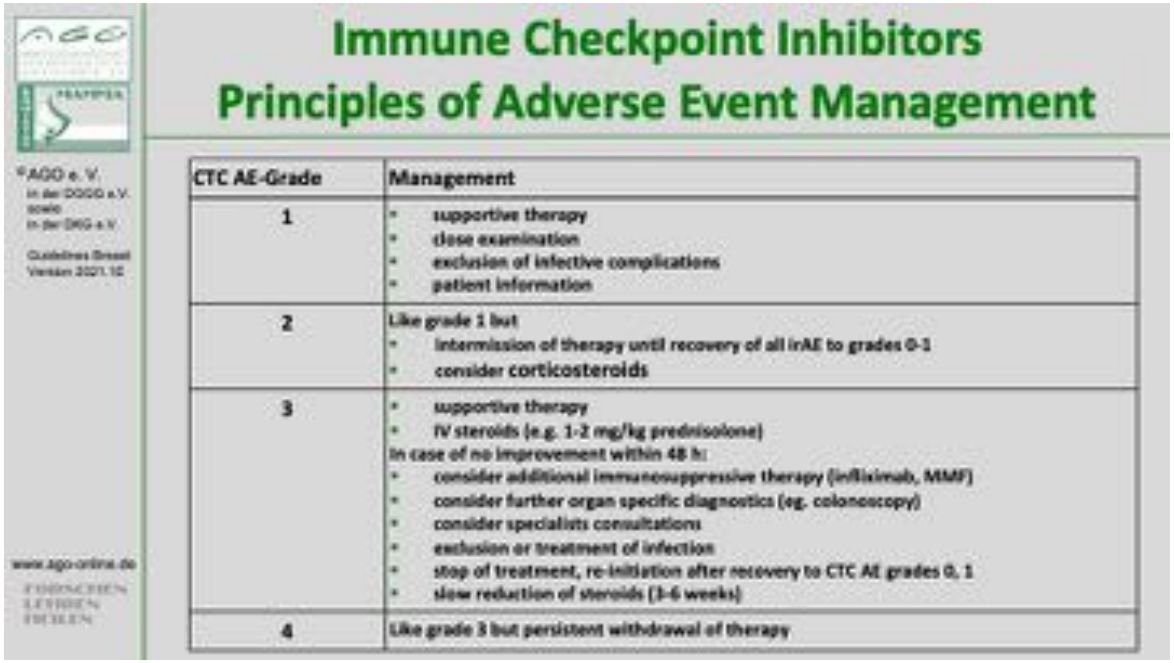


	atezolizumab	nivolumab	pembrolizumab
diarrhea	18.6%	13%	18%
colitis	1.1%	2%	1%
exanthema	18.6%	15%	<1%
hepatoxicity	0.3%	1%	0.5%
hypophysitis	<0.1%	<1%	0.5%
pneumonitis	3.1%	3%	2.9%
thyroid dysfunction	hyper- 1.7% hypo- 4.7%	hyper -1% hypo- 4%	hyper- 1.2% hypo- 8.3%
nephritis	<1%	1%	0.7%
neuropathy	0.2%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

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

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



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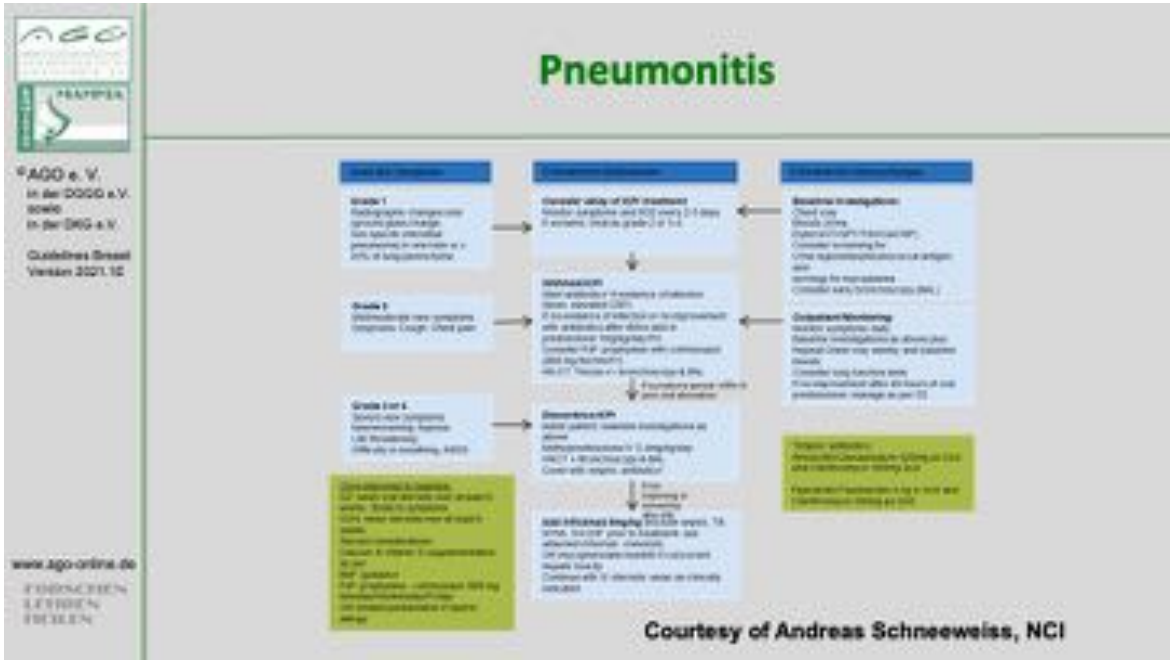

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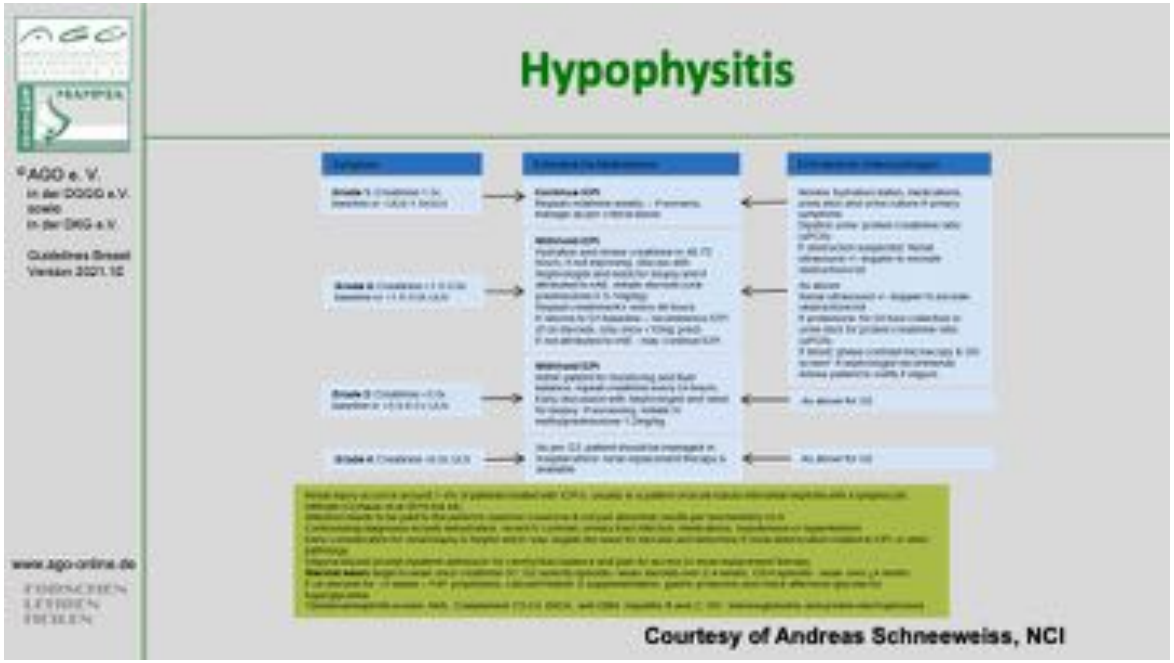

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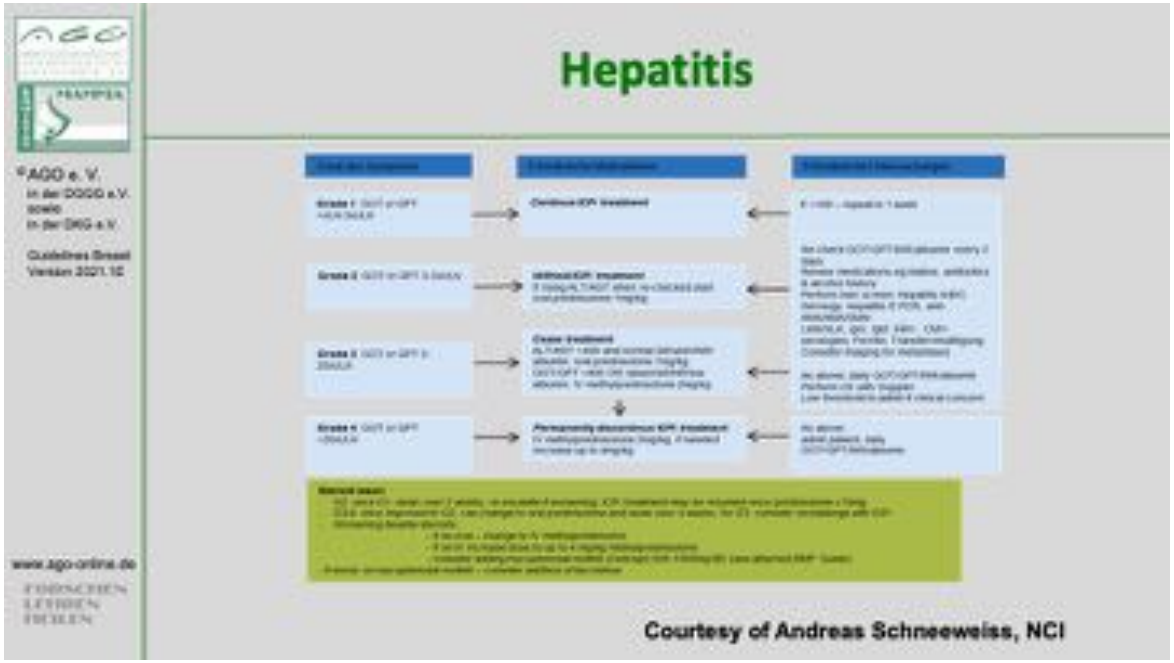

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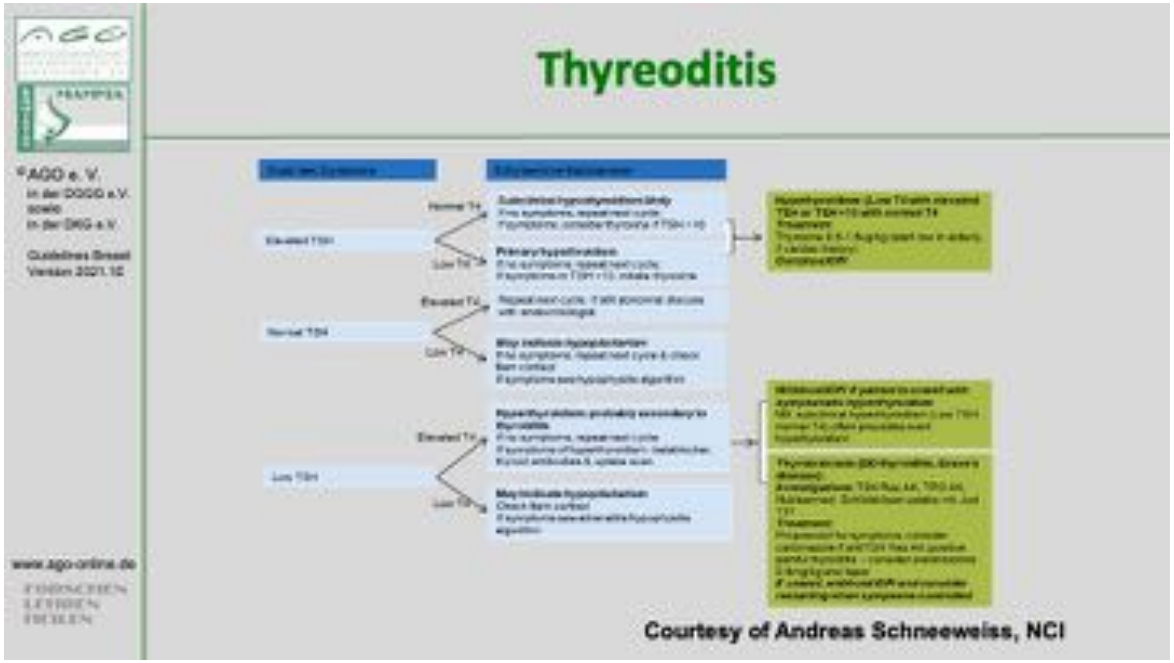

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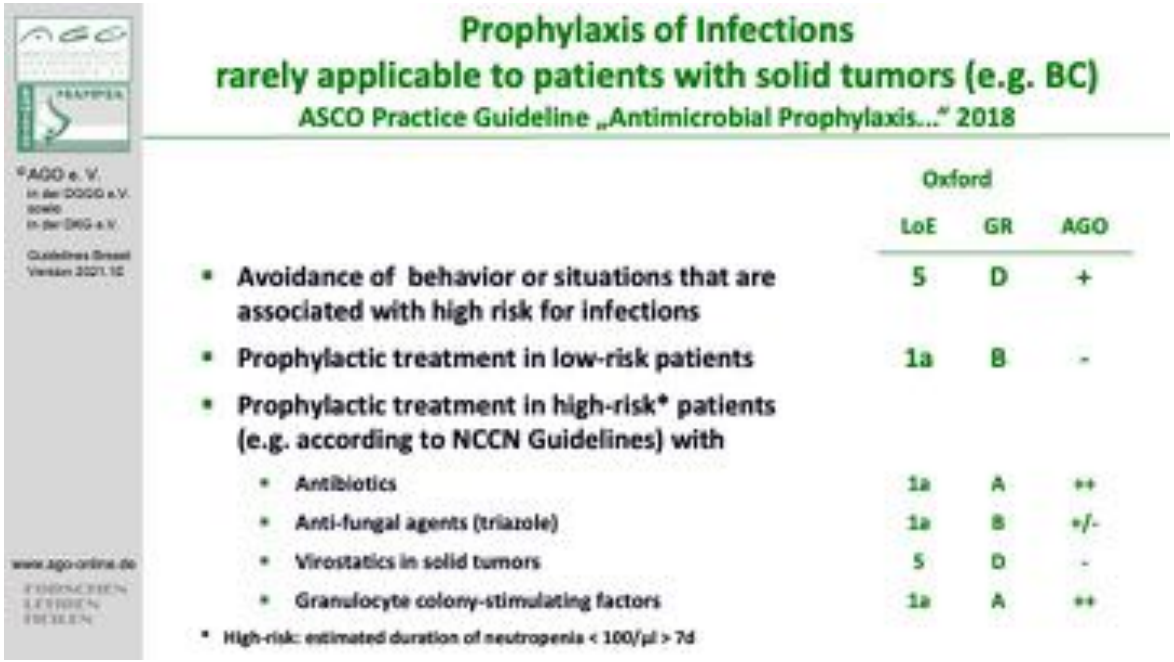
Side effects according Organ Systems

Incidence, Prevention, Therapy

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



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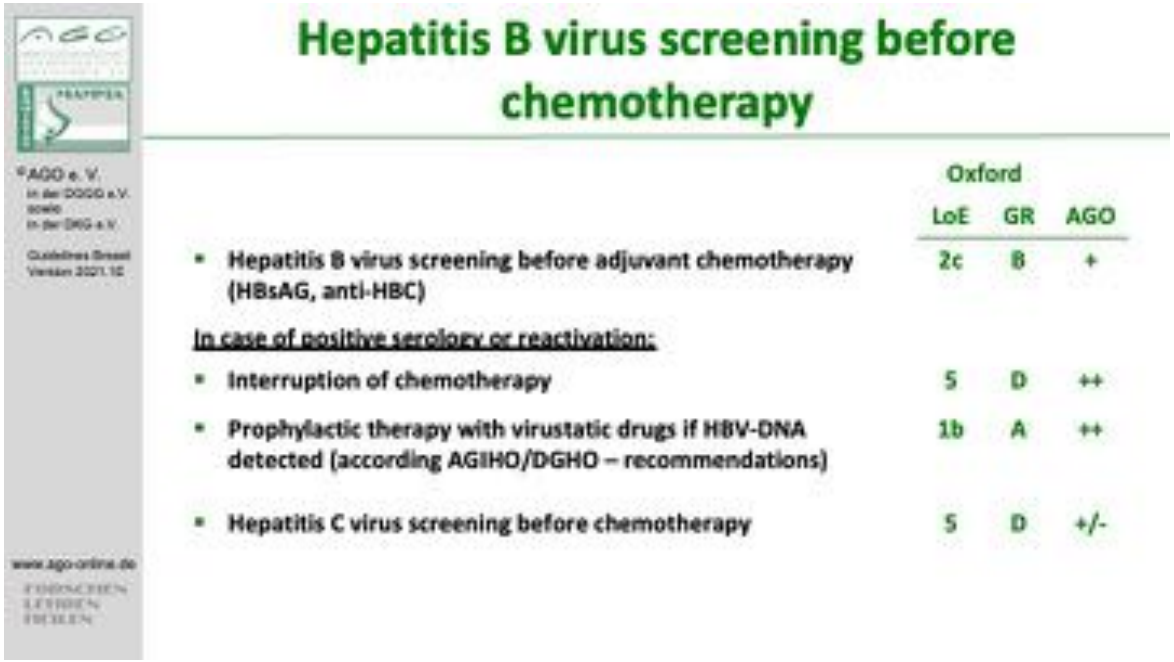

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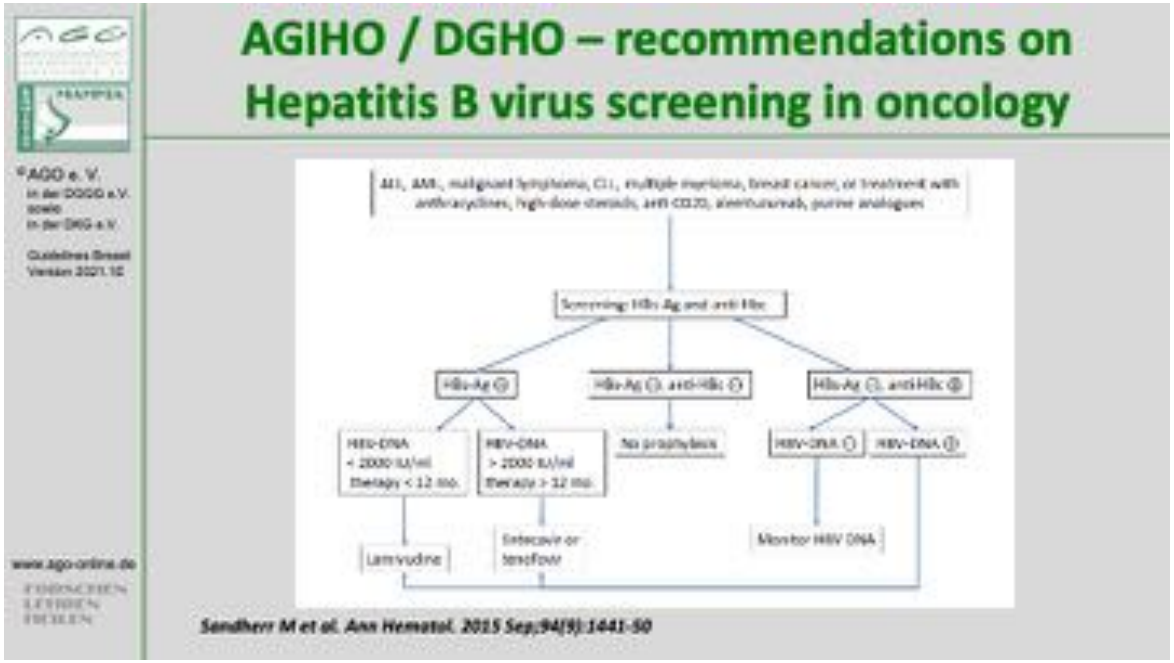

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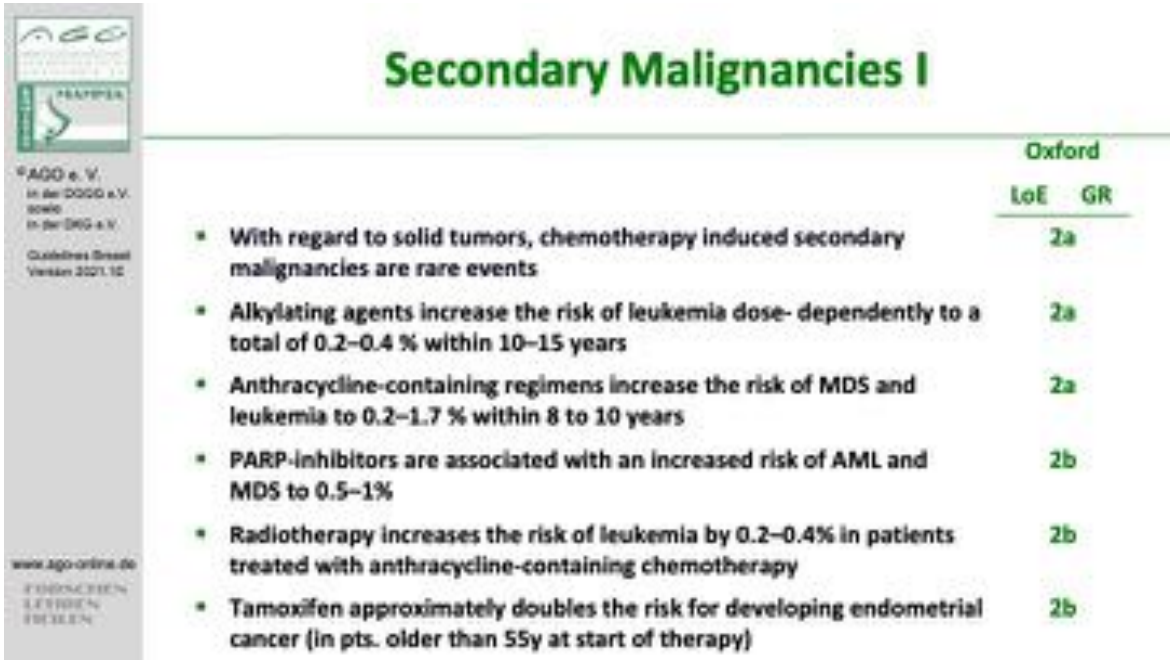
Side Effects According Organ Systems
Incidence, Prevention, Therapy

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



Statements 1-4

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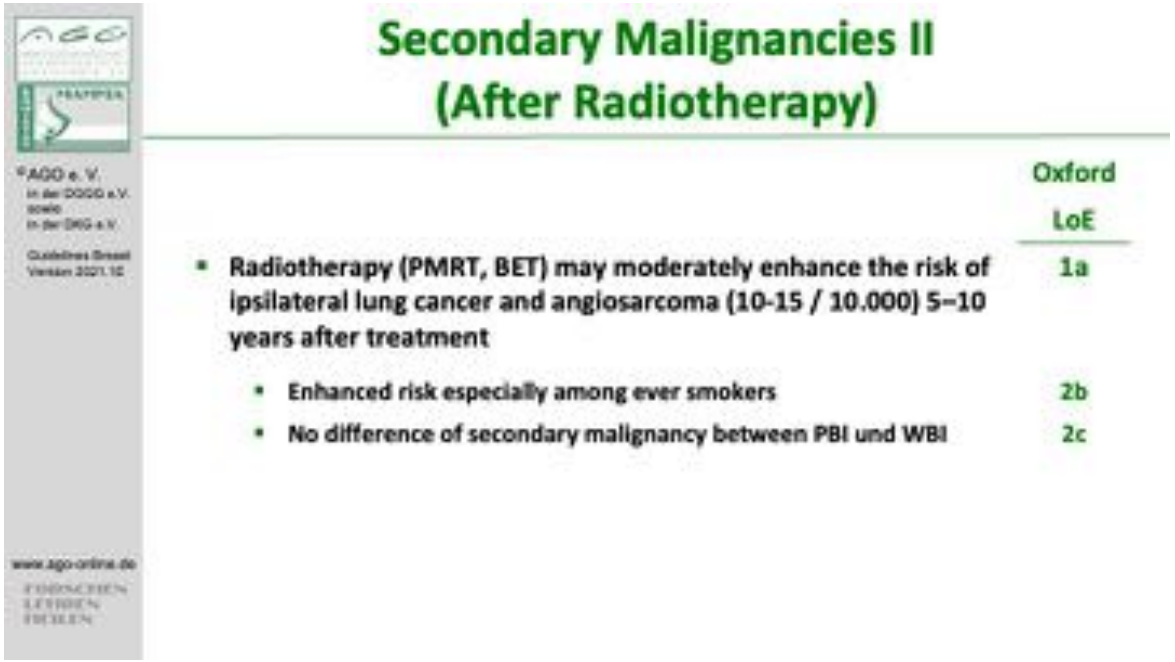

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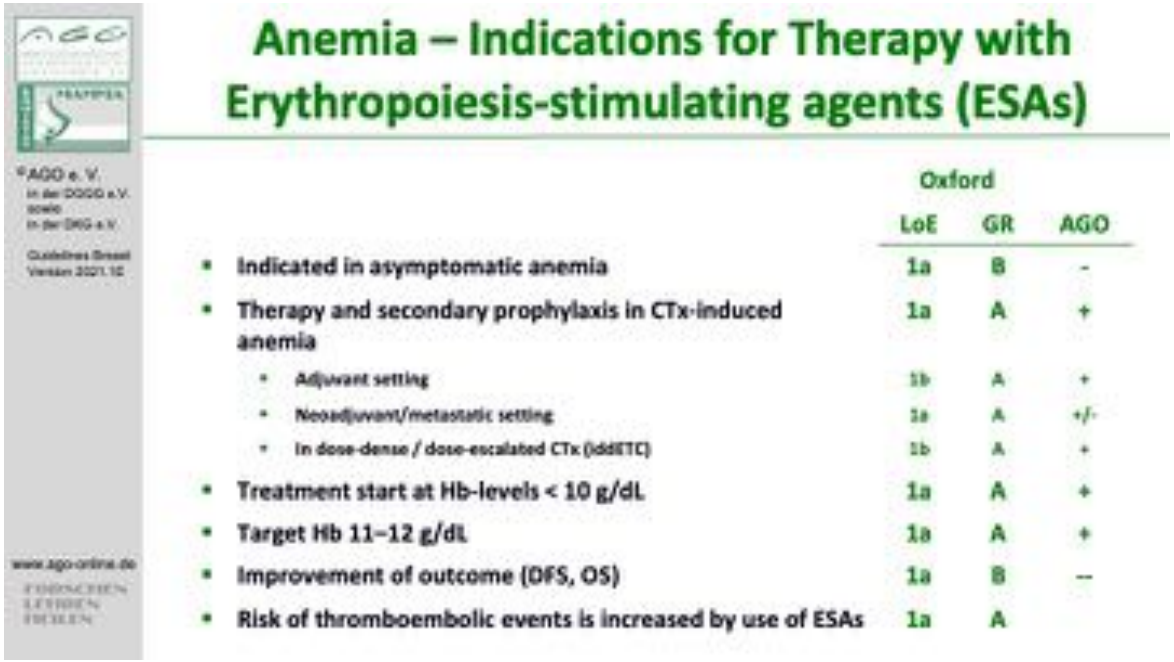
Side Effects According Organ Systems

Incidence, Prevention, Therapy

3. *Blood and Lymphatic System Disorders*

- **Anemia**
- **Neutropenia**
- **Febrile Neutropenia (FN)**



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

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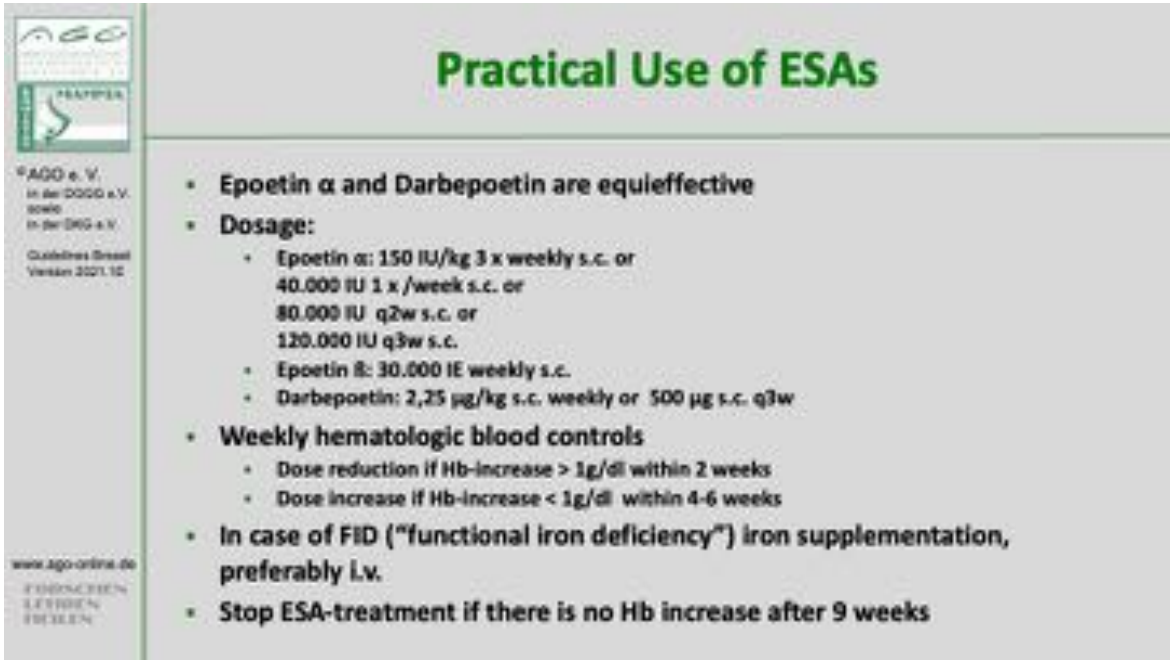

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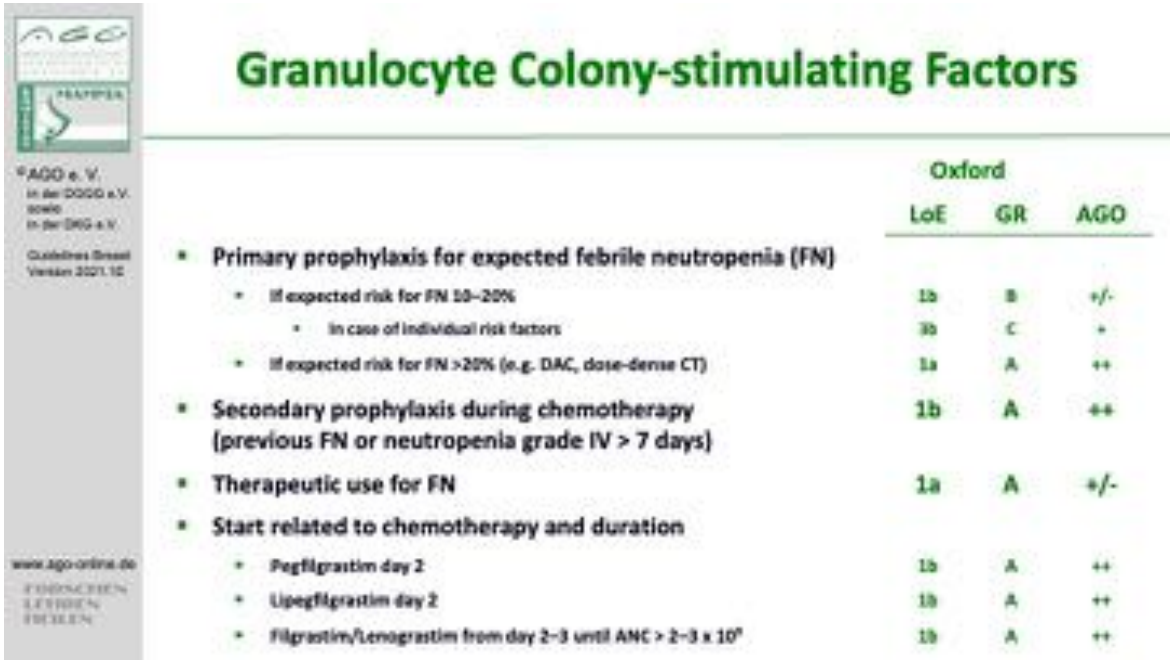

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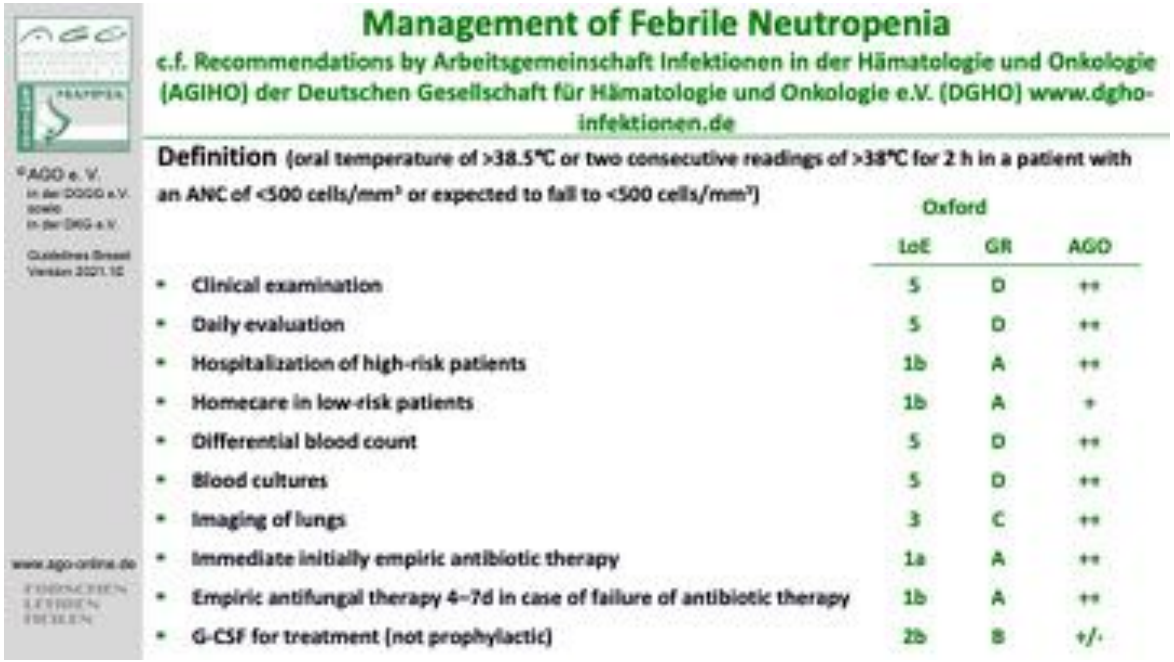

Management of Febrile Neutropenia

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

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

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

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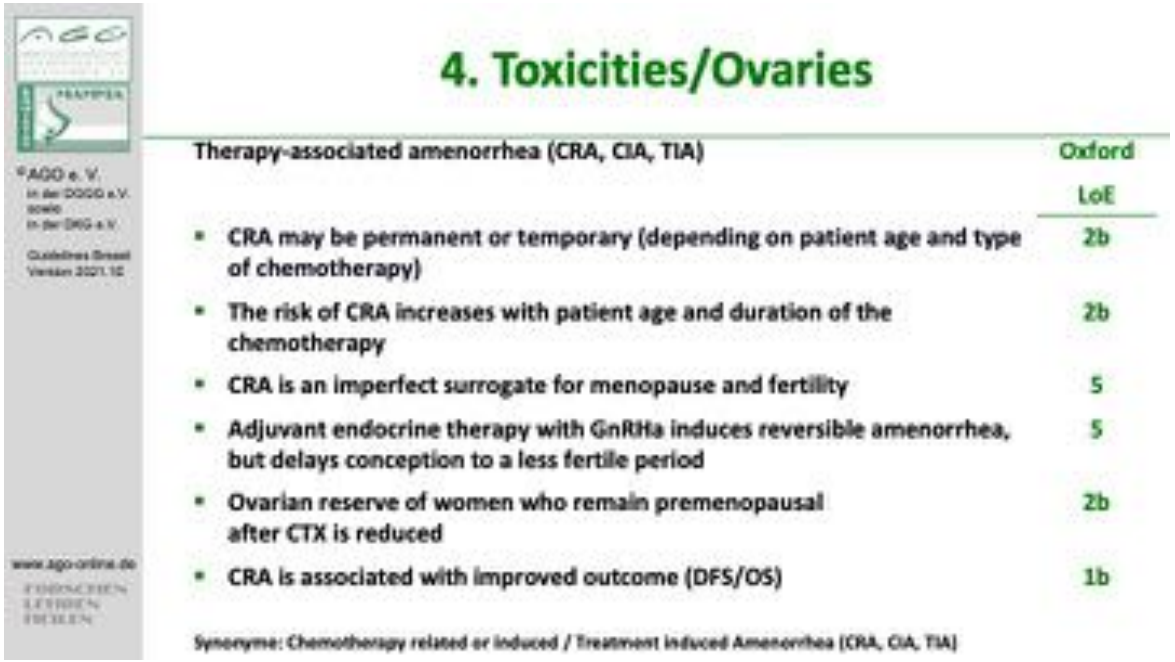

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Side Effects According Organ Systems

Incidence, Prevention, Therapy

5. Psychiatric Disorders

- Depression
- Fatigue
- Cognitive impairment
- Sleep disturbances

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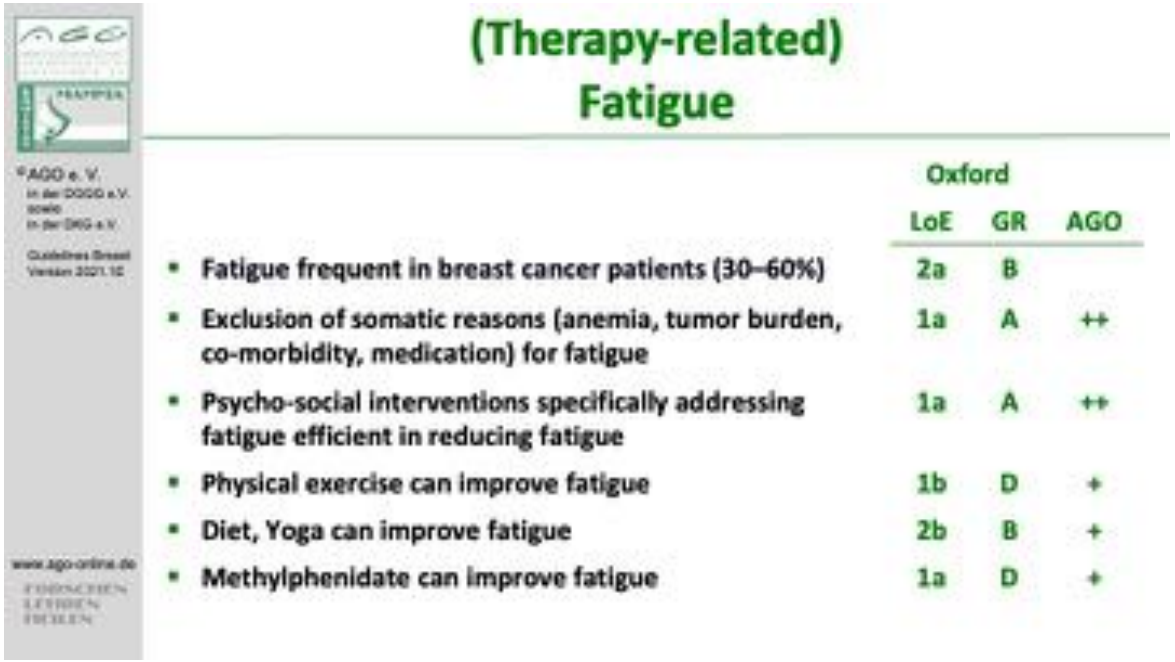

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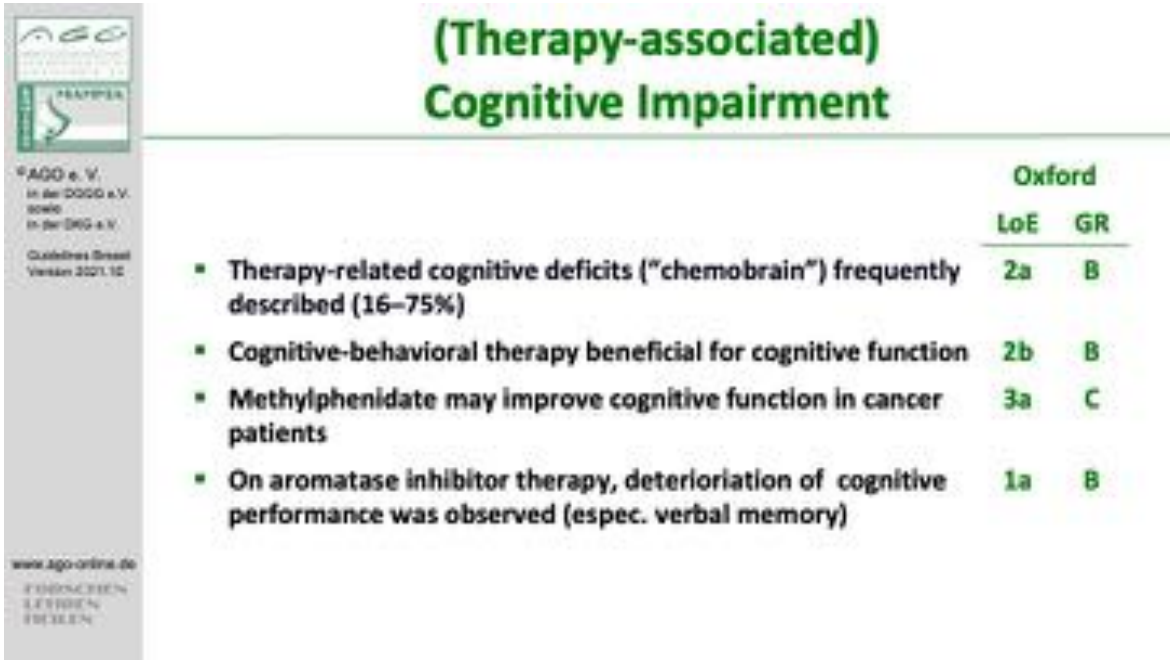

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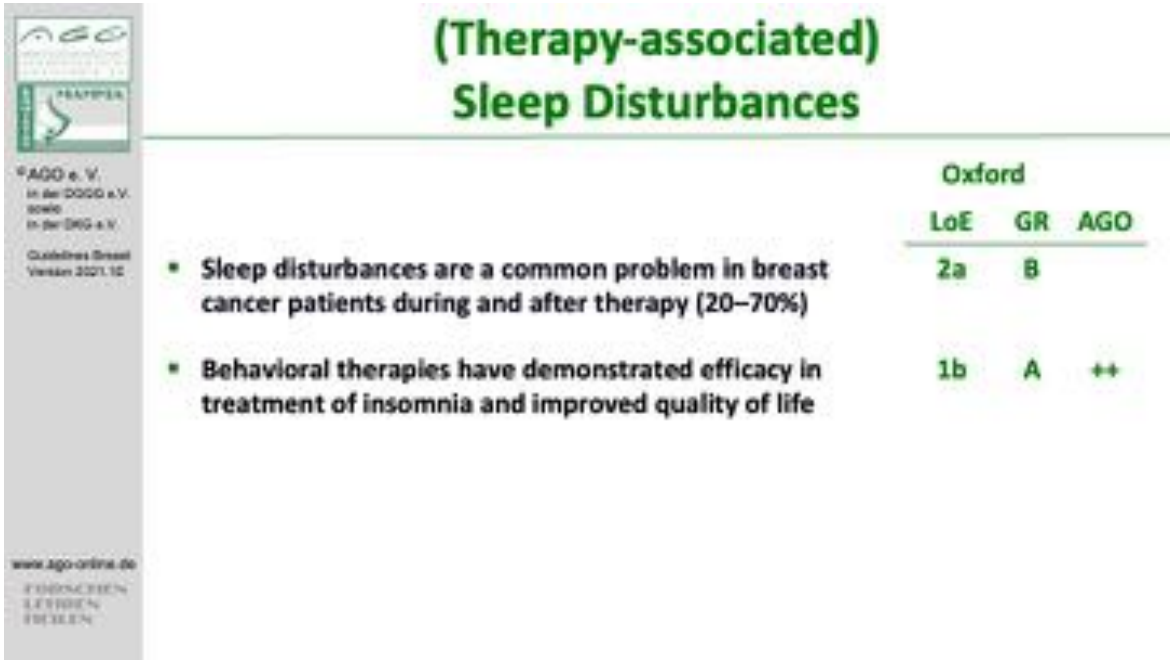

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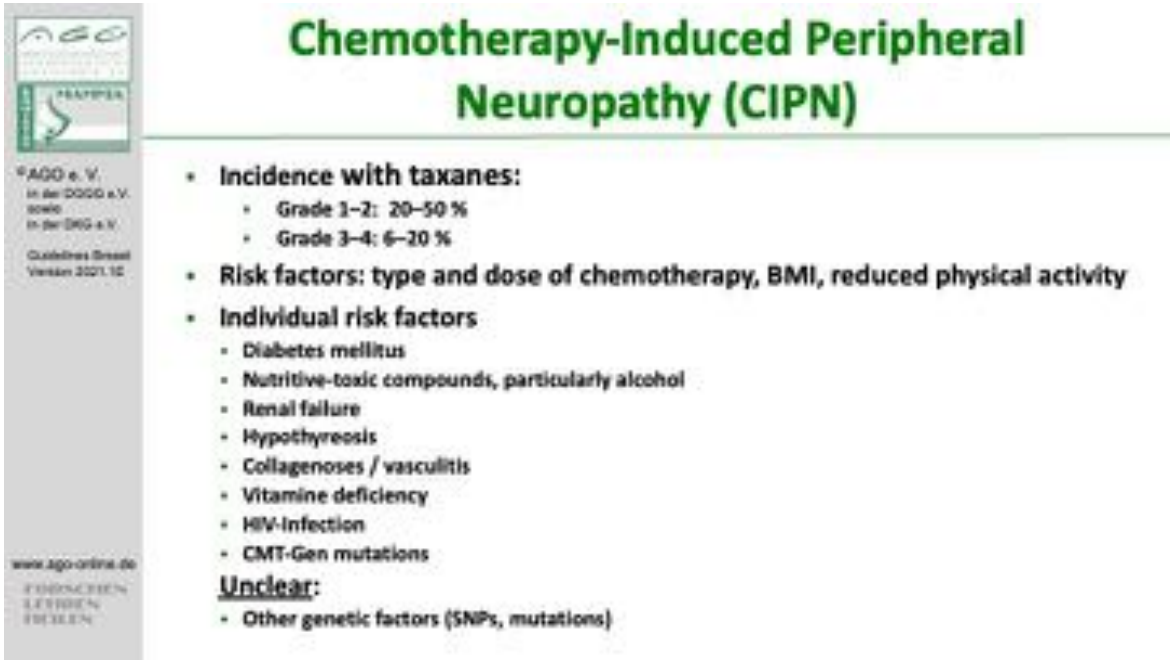
Side Effects According Organ Systems

Incidence, Prevention, Therapy

6. Nervous system disorders

- Chemotherapy-Induced Peripheral Neuropathy (CIPN)



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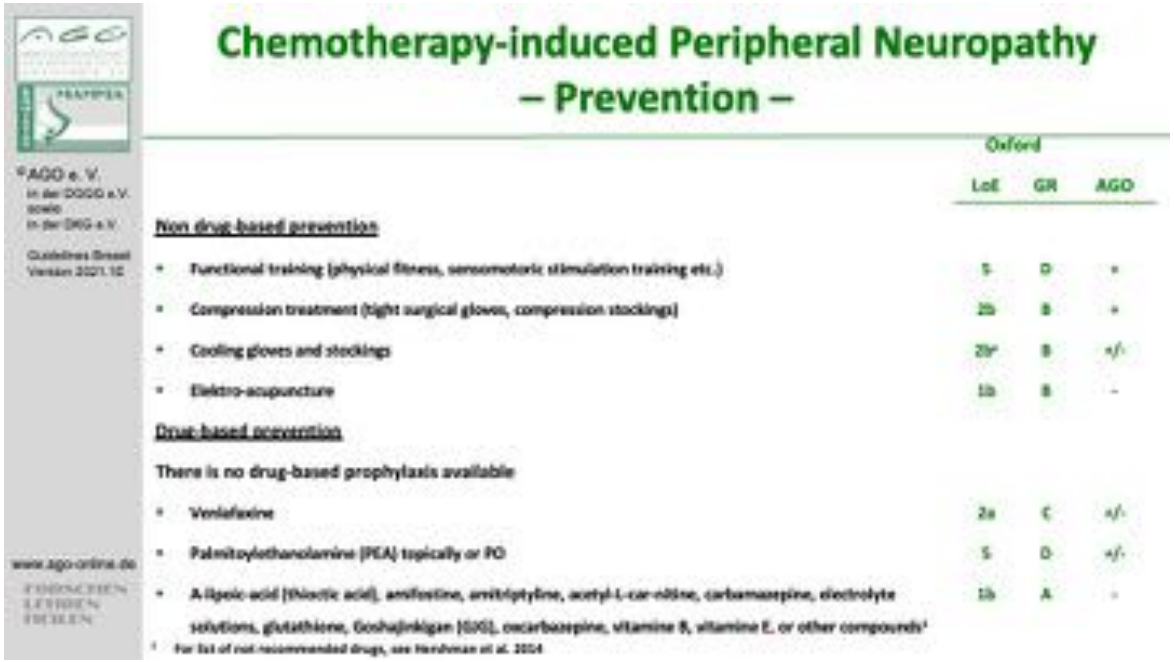

Chemotherapy-induced Peripheral Neuropathy
– Prevention –

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	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*	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	+/-
• Alpha-lipoic acid (thioctic acid), amifostine, amitriptyline, acetyl-L-carnitine, 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

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Kompression

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Kühlung

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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

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Nicht-medikamentöse Therapie

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Medikamentöse Therapie

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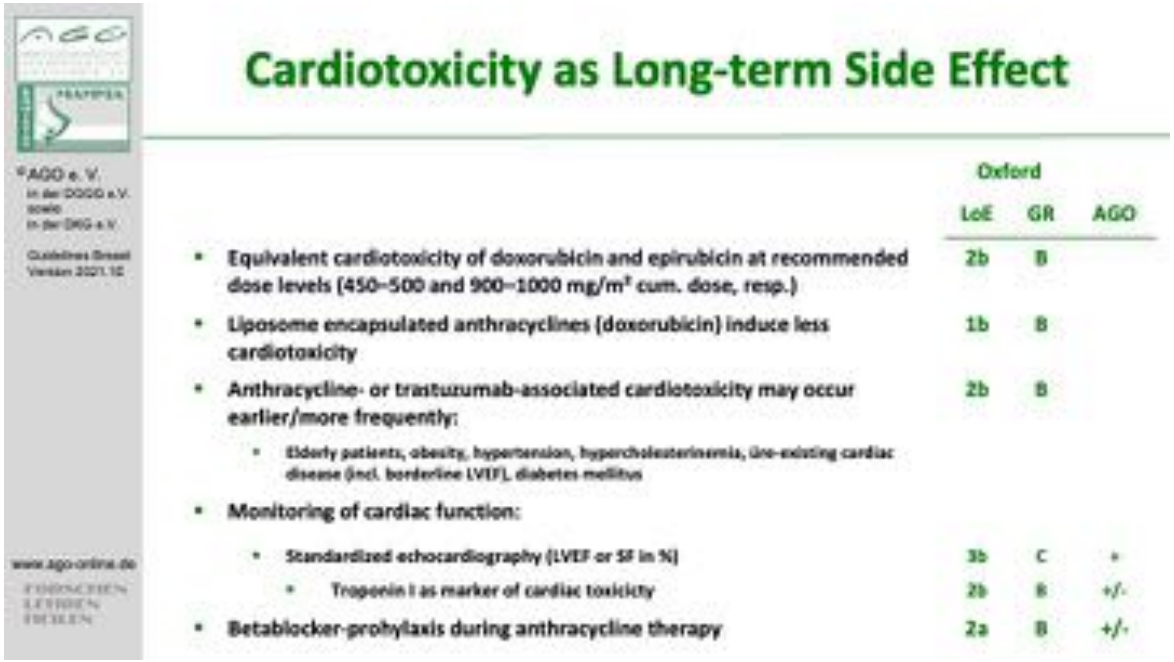
Side Effects According Organ Systems

Incidence, Prevention, Therapy

7. Cardiac Disorders



Statements

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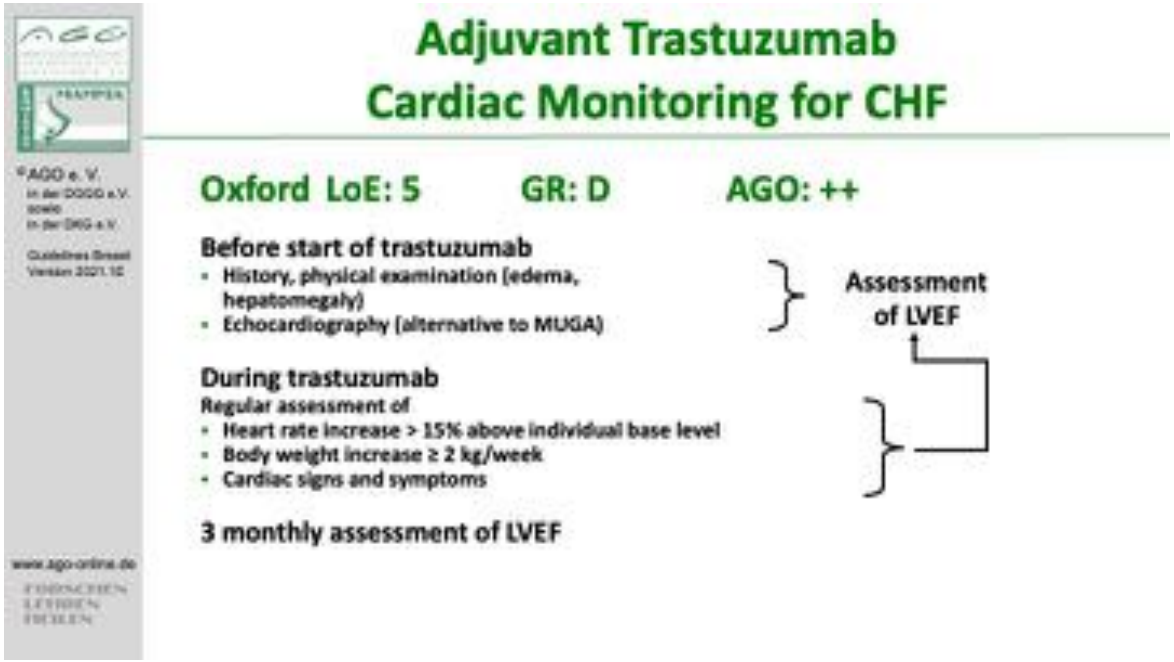

Statement: Cardiac Monitoring (5 D ++)

Vote result of the AGO recommendation: 100%

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"Anthracycline simultaneous to radiotherapy"

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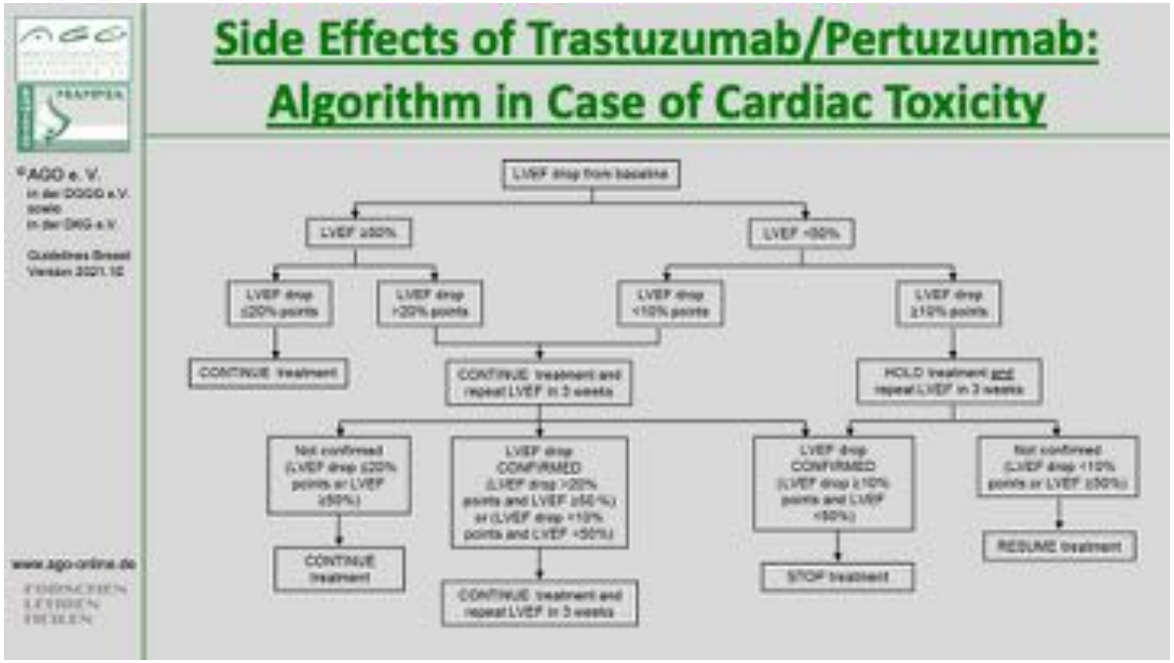

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Side Effects According Organ Systems

Incidence, Prevention, Therapy

8. Gastrointestinal Disorders

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

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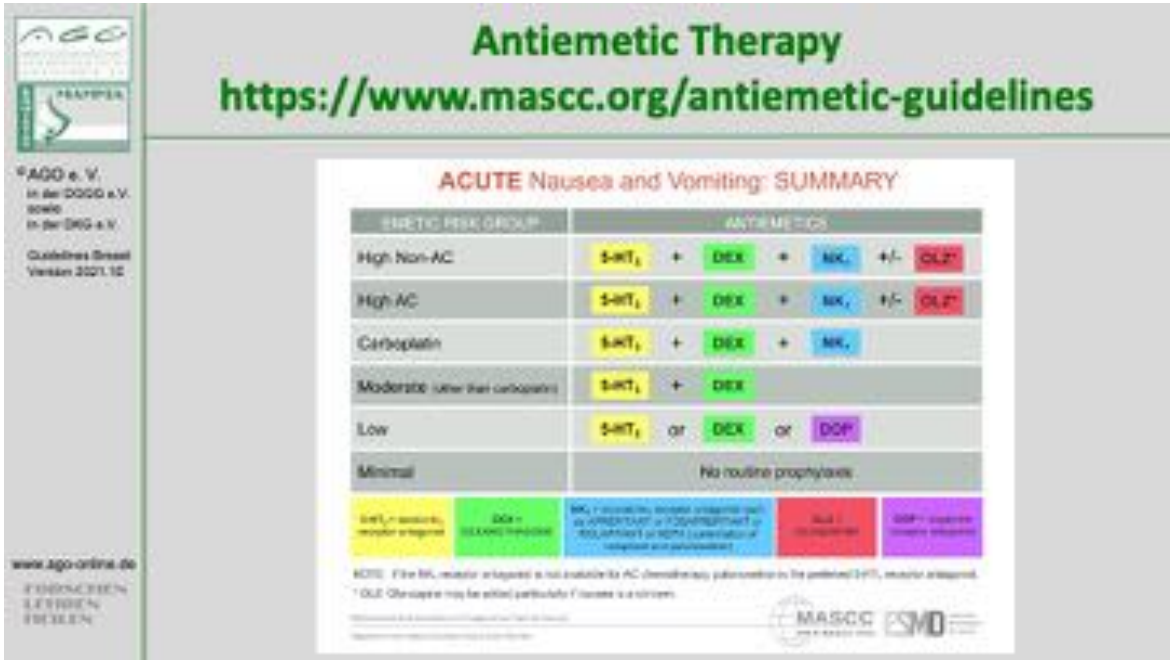

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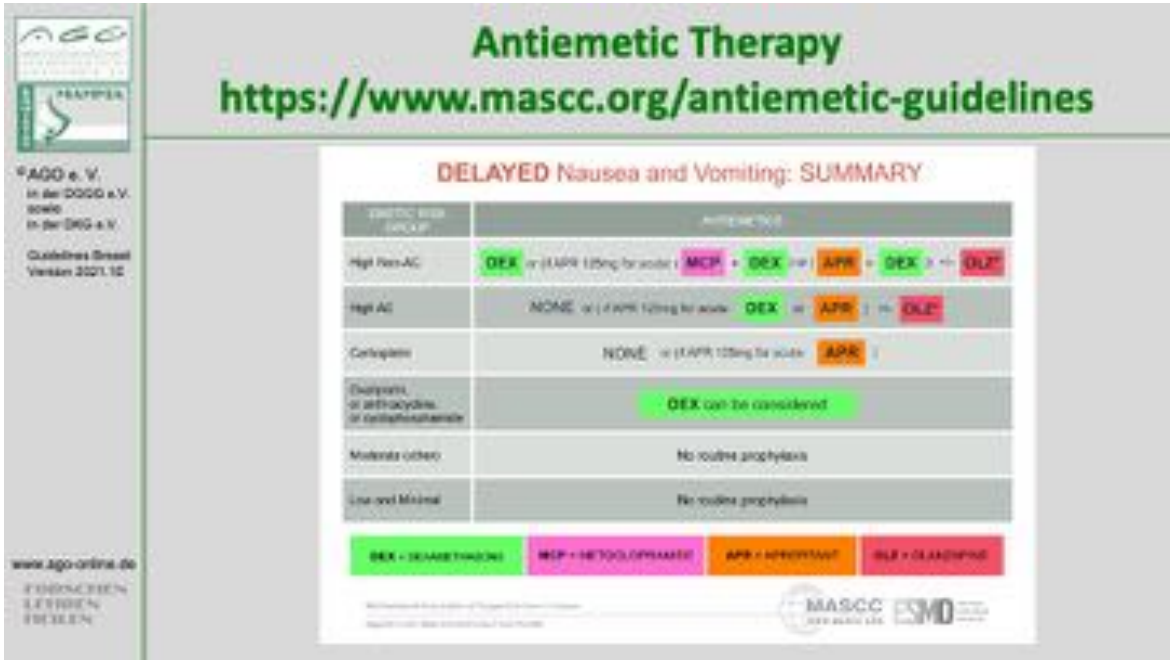

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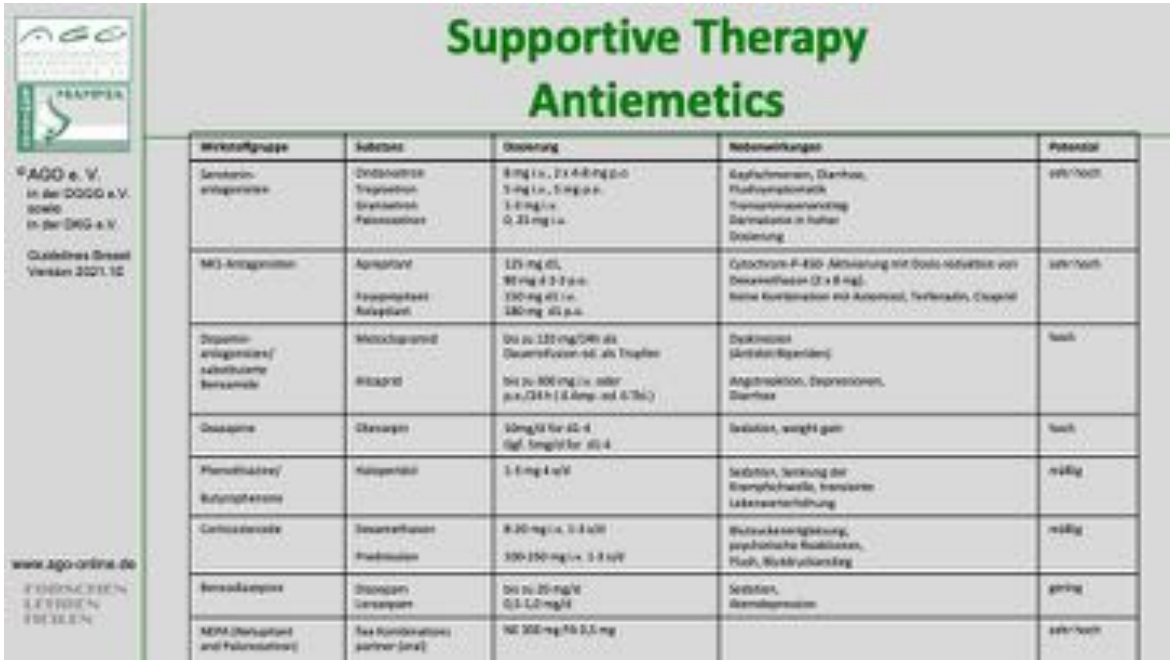

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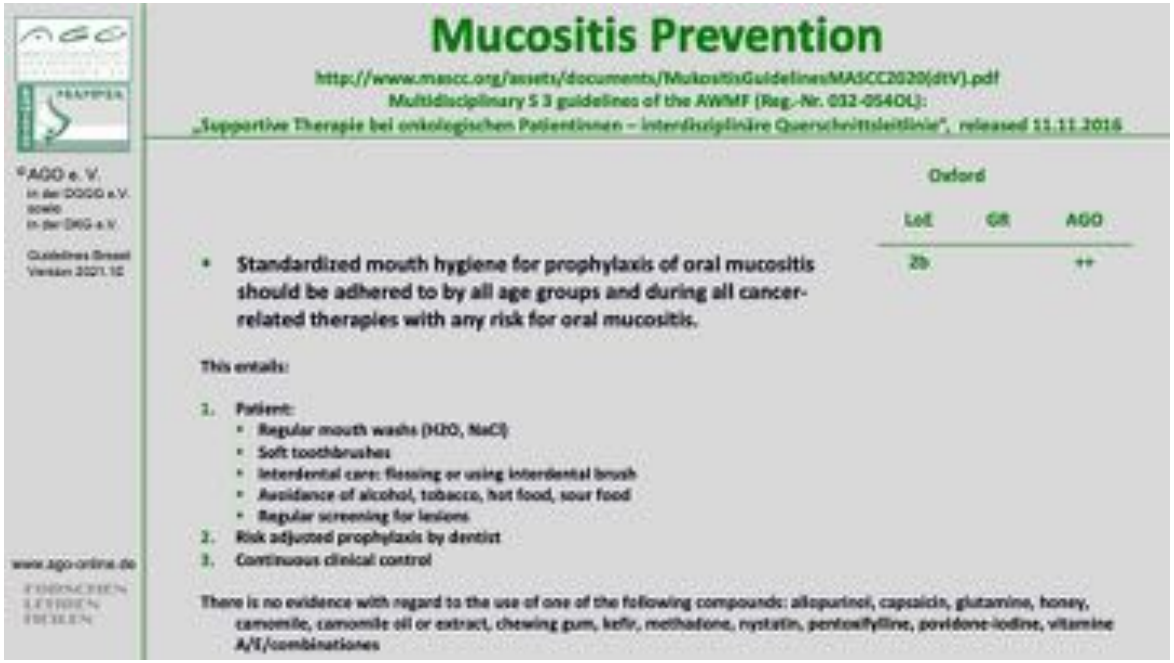

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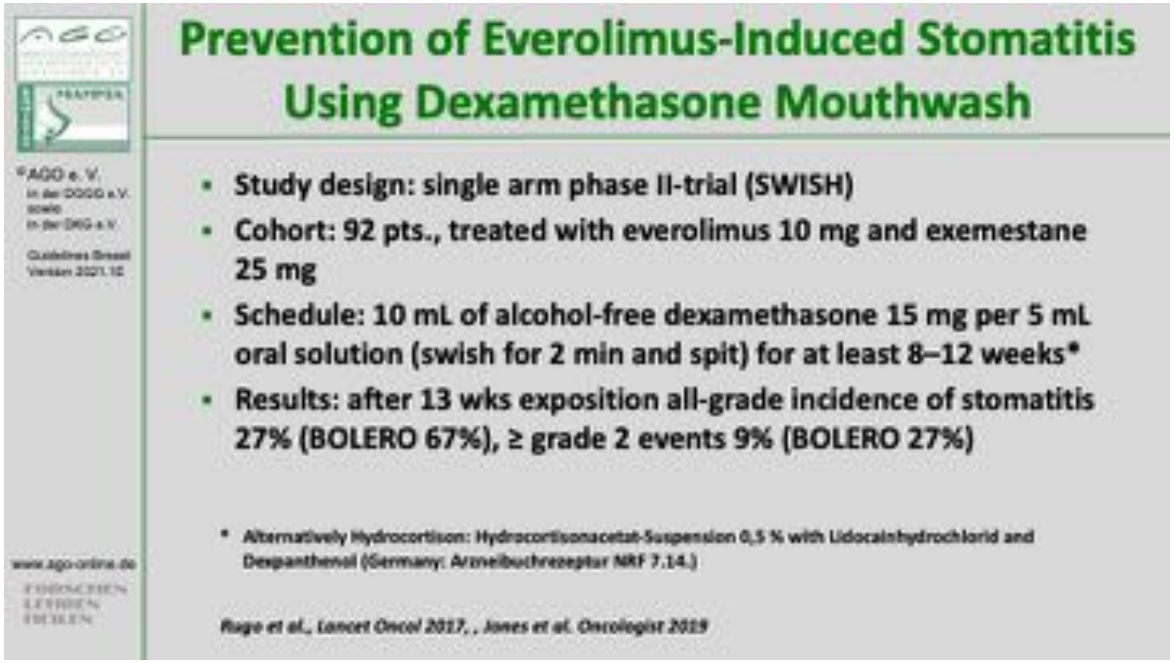

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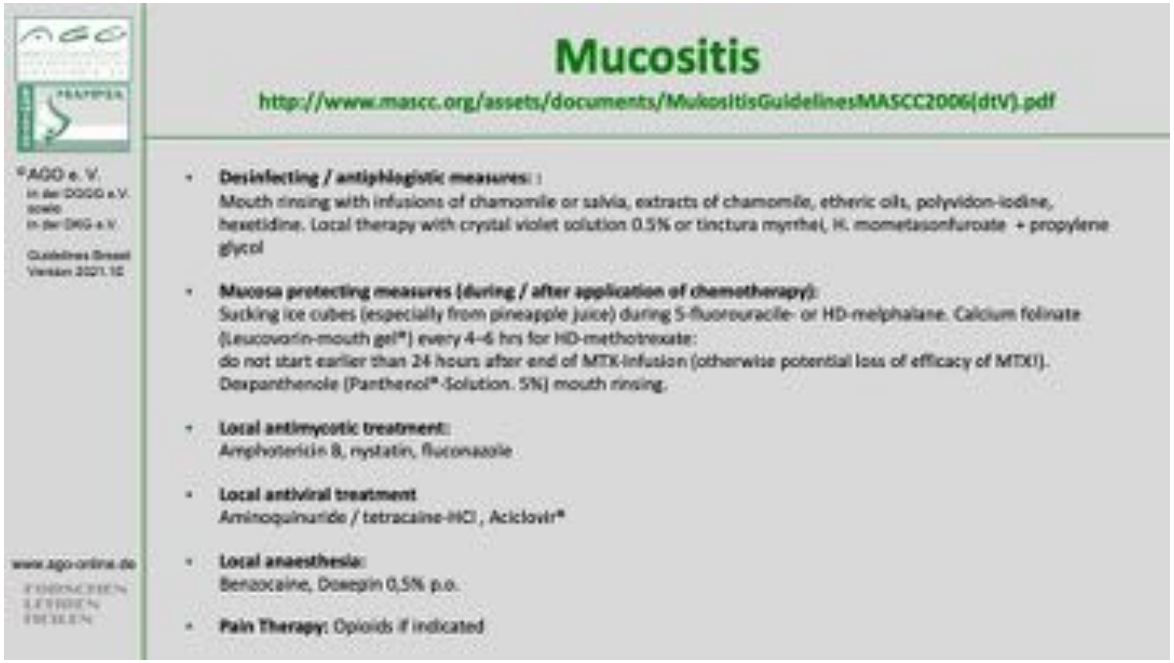

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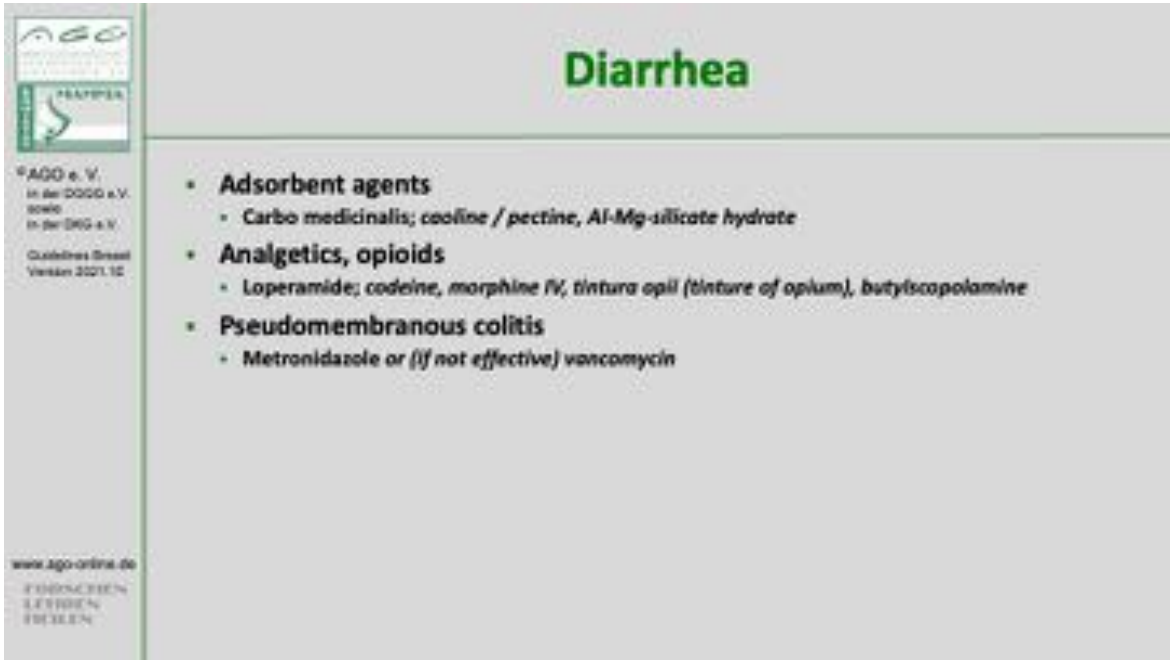

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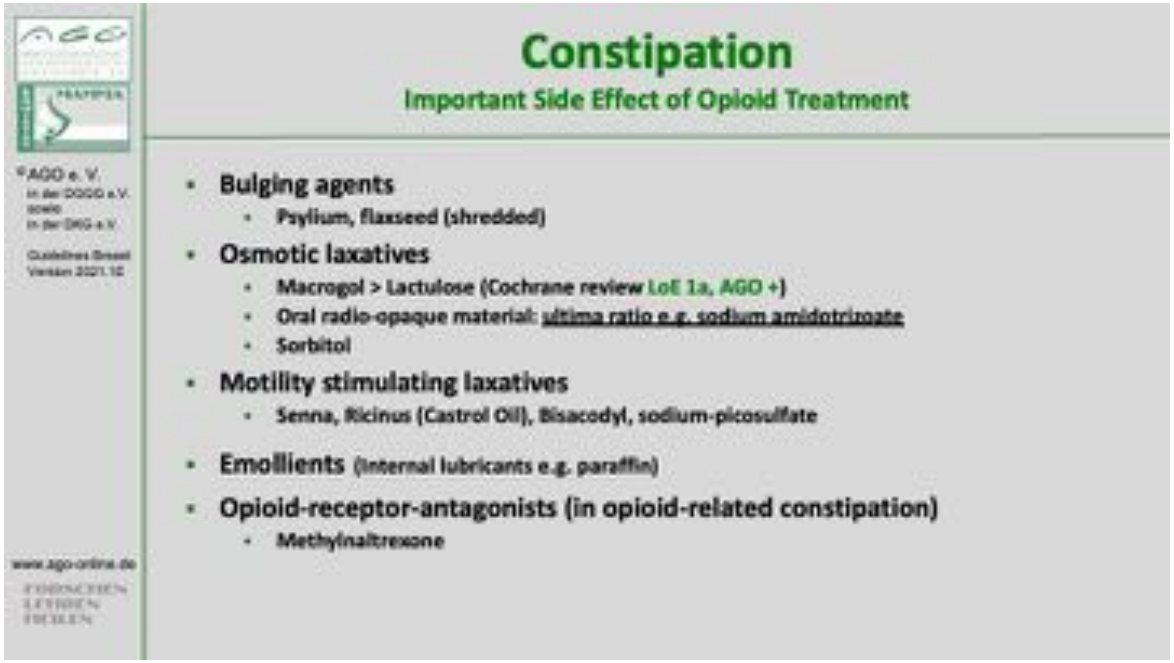

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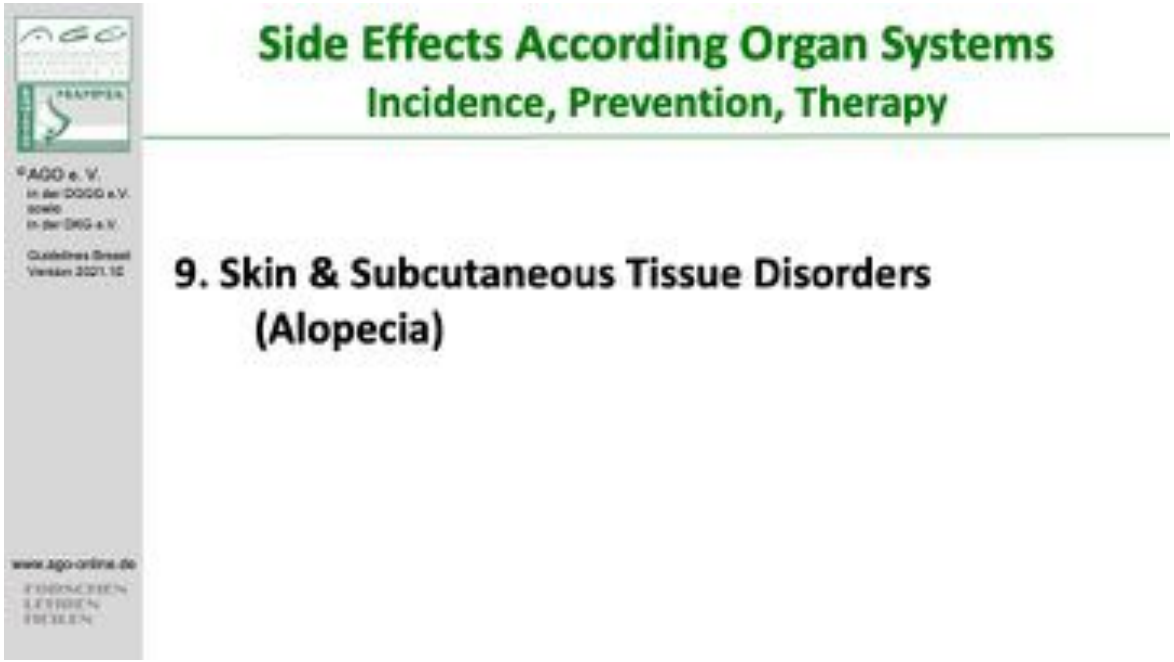

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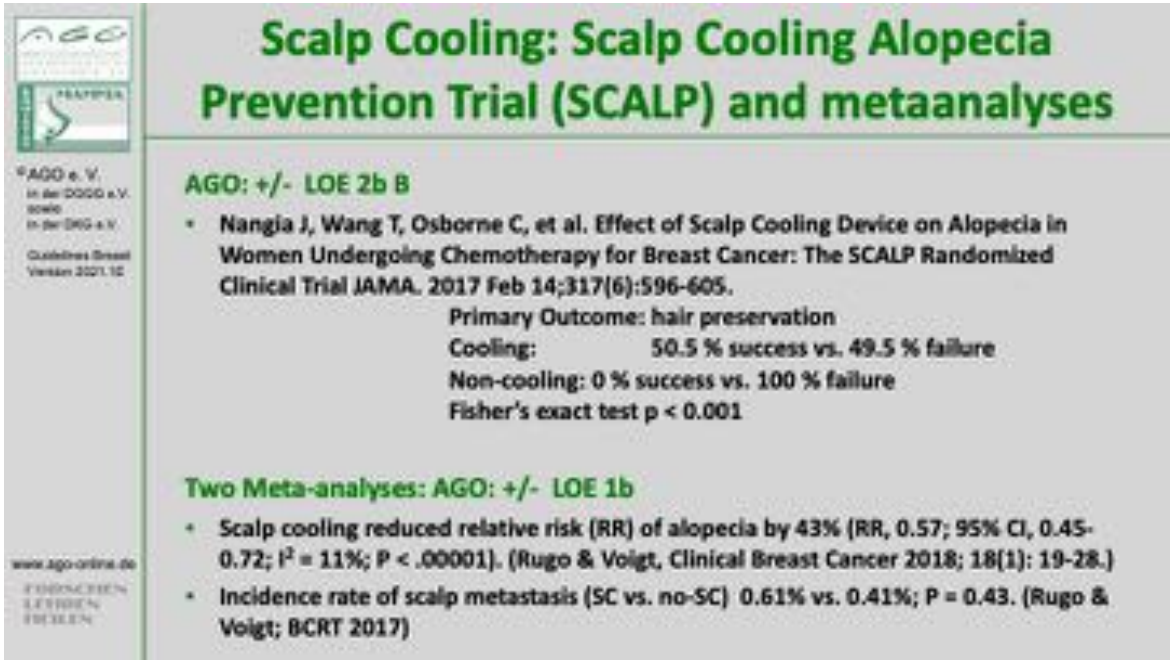

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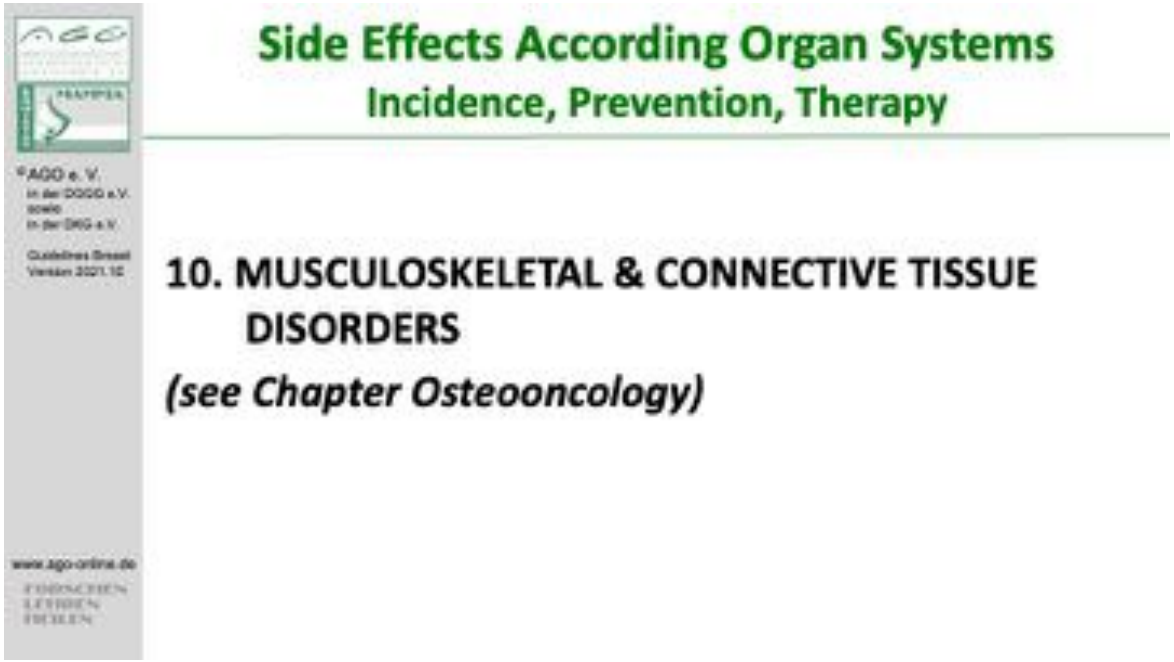

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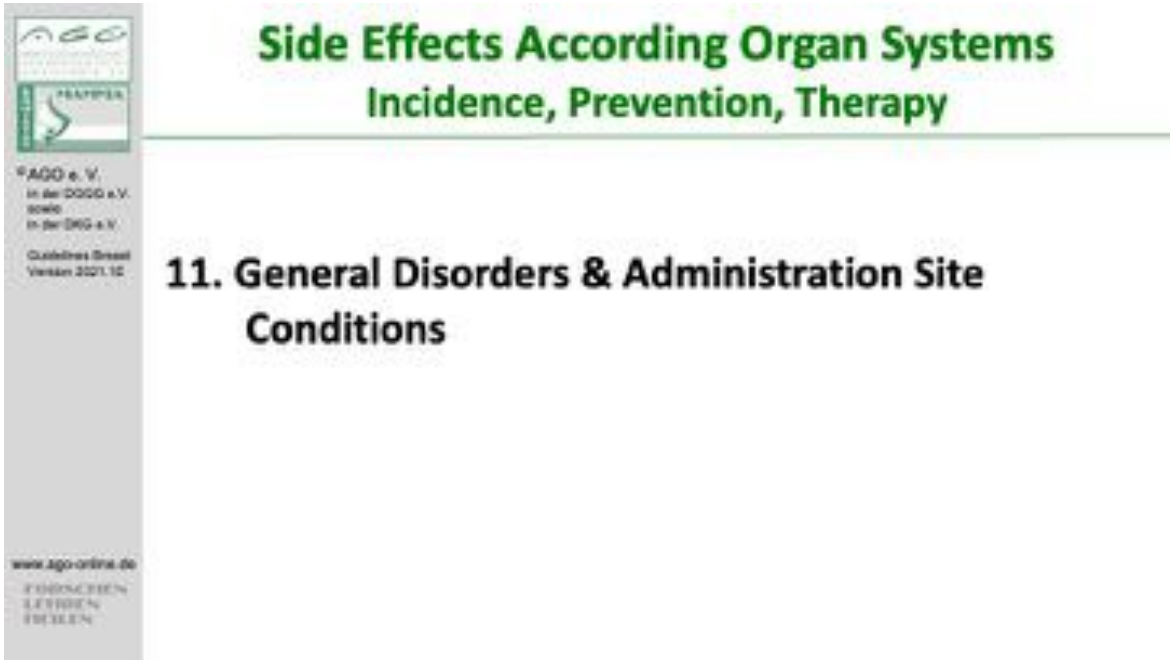

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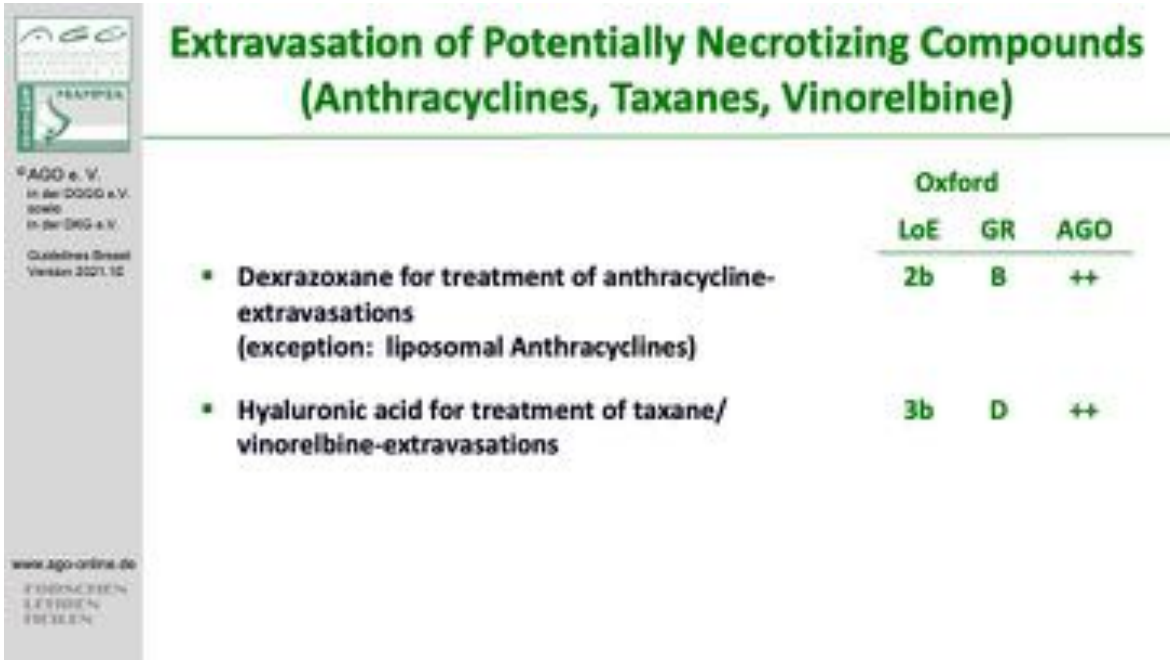

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Hyaluronsäure

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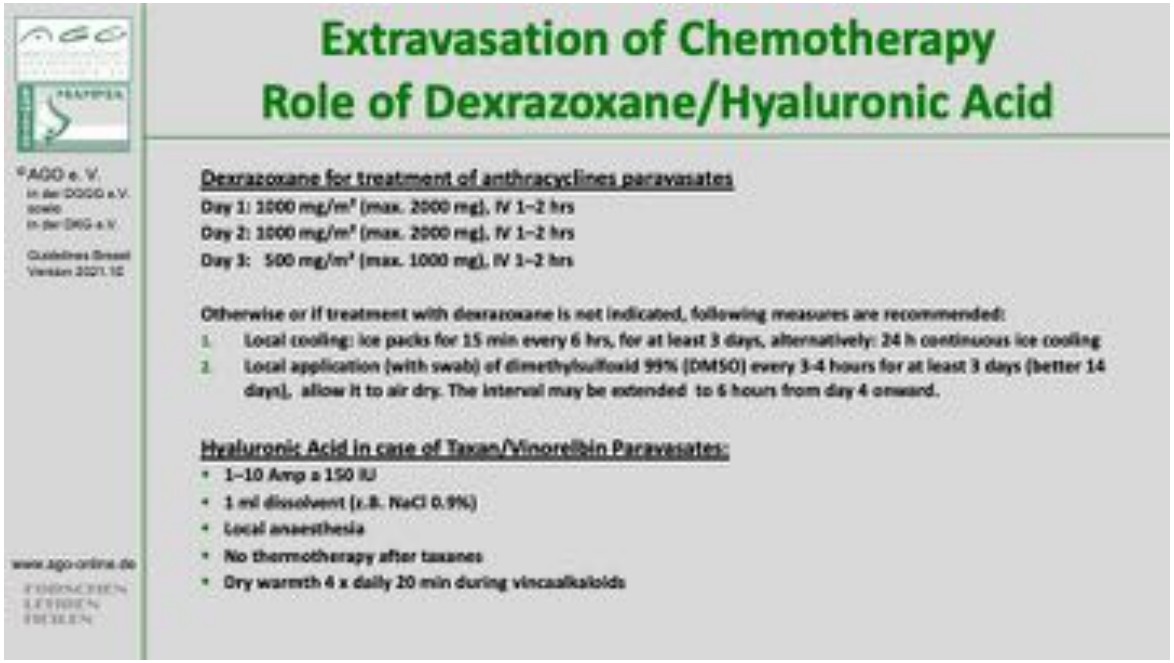

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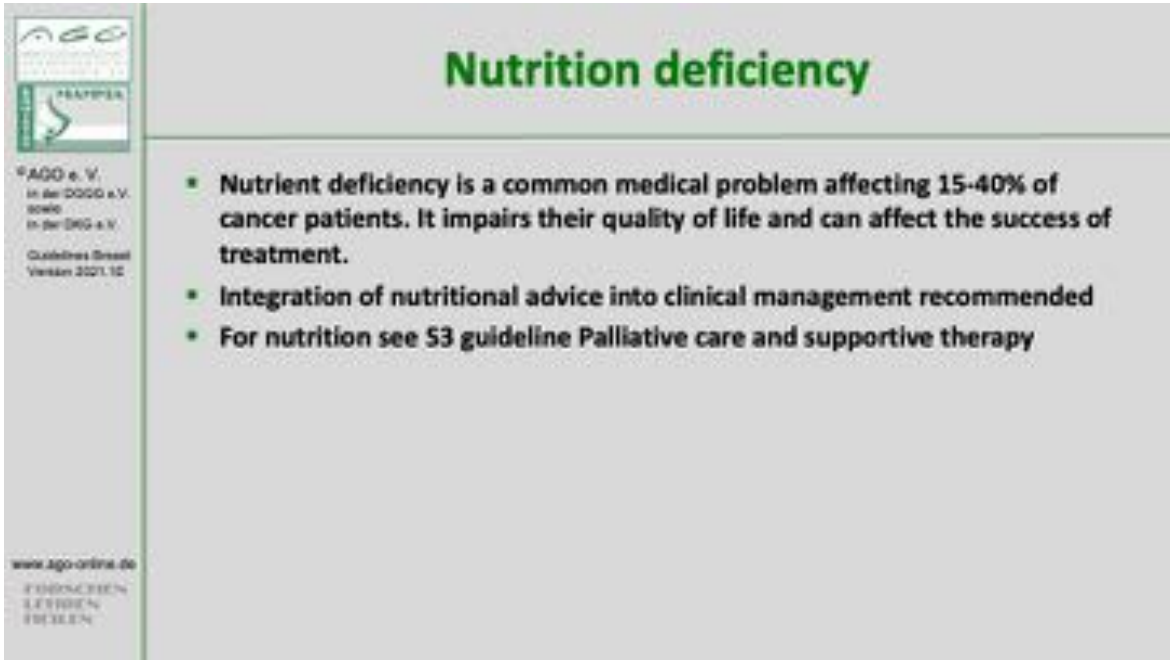
- **Further supportive and palliative issues**
  - **Nutrition**
  - **Pain management**
  - **Palliative Care**



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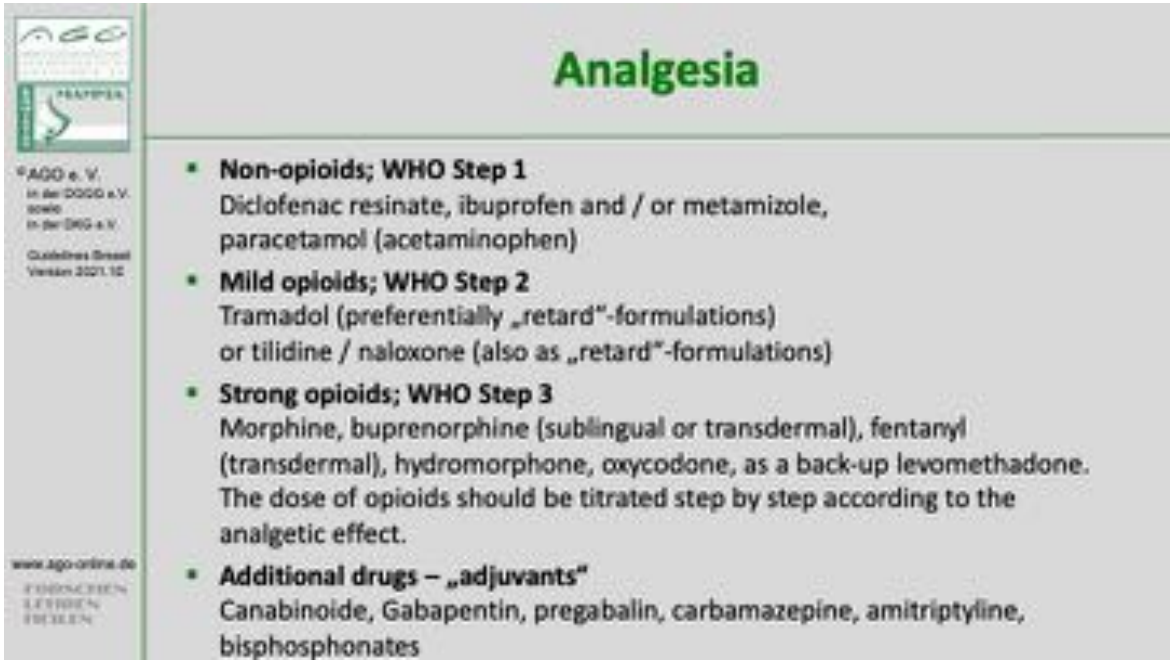

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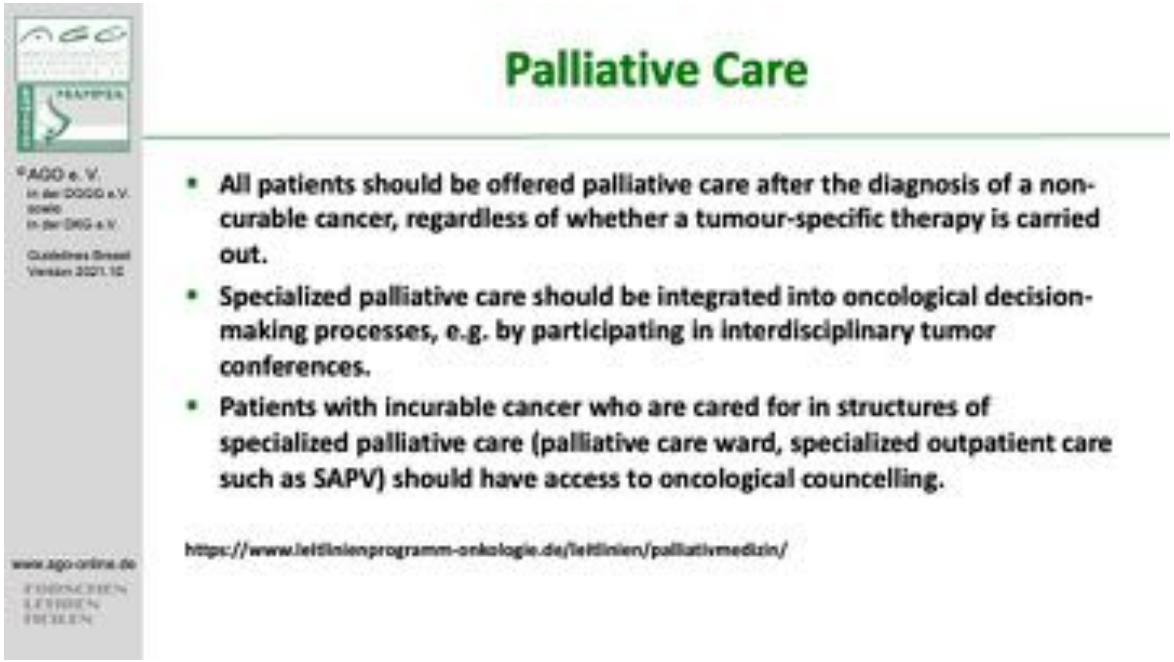

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