Guidelines Breast
Version 2017.1

Supportive Care

Supportive Care

- **Version 2002:**
  Diel

- **Versions 2003–2016:**
  Bauerfeind / Bischoff / Costa / Dall / Diel / Fersis / Hanf / Heinrich / Jackisch / von Minckwitz / Möbus / Oberhoff / Rody / Schaller / Scharl / Schmidt / Schütz

- **Version 2017:**
  Möbus / Nitz

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Version 2017.1

Guideline Spectrum

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 „Arbeitsgem. Supportive Maßnahmen in der Onkologie, Rehabilitation und Sozialmedizin der DKG: http://www.onkosupport.de“ should especially be highlighted.

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

„Supportive Therapie bei onkologischen PatientInnen - interdisziplinäre Querschnittsleitlinie“, released 11.11.2016

Erythropoiesis-stimulating agents (ESAs)

	Oxford / LoE / GR		AGO
➢ Indicated in asymptomatic anaemia	1a	B	-
➢ Therapy and secondary prophylaxis in CIA	1a	A	+
➢ In the adjuvant setting	1b	A	+
➢ In the neoadjuvant/metastatic setting	1a	A	+/-
➢ In dose-dense / dose-escalated CT (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	

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References

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

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Version 2017.1

N=2.098 Pat., Hb <11g/dl; non inferiority study.
Prespecified upper non inferiority margin = 1.15

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

* Investigator determined
**Independent review committee

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References

Practical Use of ESAs

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- **Epoetin α and Darbepoetin are equieffective**
- **Dosage:**
  - **Epoetin α: 150 IU/kg 3 x weekly s.c. or**
    40.000 IU 1 x /week s.c. or
    80.000 IU q2w s.c. or
    120.000 IU q3w s.c.
  - **Epoetin ß: 30.000 IE weekly s.c.**
  - **Darbepoetin: 2,25 µg/kg s.c. weekly or 500 µg s.c. q3w**
- **Hematologic blood samples weekly**
  - **Dose reduction if Hb-increase > 1g/dl within 2 weeks**
  - **Dose increase if Hb-increase < 1g/dl within 4-6 weeks**
- **In case of FID (“functional iron deficiency”) iron supplementation, preferably i.v.**
- **Stop ESA-treatment if there is no Hb increase after 9 weeks**

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Further Information

References

Relevant Guidelines

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

Granulocyte Colony-stimulating Factors

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	Oxford / LoE / GR	AGO	
➢ **Primary prophylaxis for expected febrile neutropenia (FNP)**			
➢ **If expected risk for FNP 10–20%**	1b	B	+/-
➢ **In case of individual risk factors**	3b	C	+
➢ **If expected risk for FNP >20% (e.g. DAC, dose-dense CT)**	1a	A	++
➢ **Secondary prophylaxis during chemotherapy (previous FNP or neutropenia grade IV > 7 days)**	1b	A	++
➢ **Therapeutic usage for FNP**	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	++

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 (H. Link et al: 04/07)

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 initial 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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Further Information

References

Empirical Antibiotic Therapy

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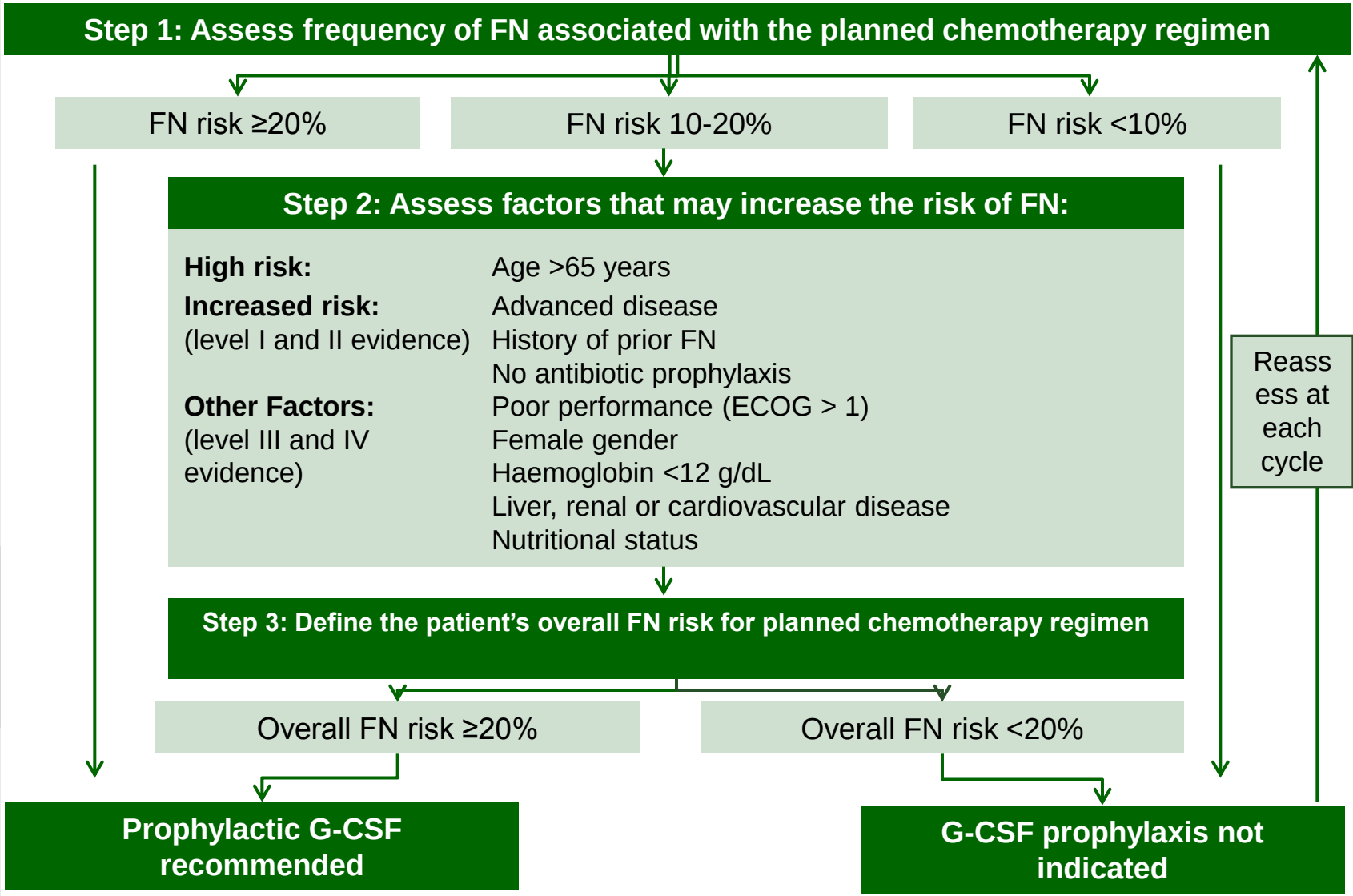
The recommendations for empirical antibiotic therapy are currently changing because of infection biological findings. Current recommendations should be referred to regularly and adjusted to within personal professional judgement.

The “Arbeitsgemeinschaft Infektionen in der Hämatologie und Onkologie (AGIHO) der Deutschen Gesellschaft für Hämatologie und Onkologie e.V. (DGHO) www.dgho-infektionen.de“ is a source for regular consultation.

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



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Version 2017.1

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Further Information

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Relevant Guidelines

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Version 2017.1

- Crawford et al: Myeloid Growth Factors. J Natl Compr Canc Netw:1266-1290, 2013
- Thomas J. Smith, Kari Bohlke, Gary H. Lyman et al. Recommendations for the use of WBC Growth factors: American society of clinical practice guideline update. J Clin Oncol 2015;28:3199-3212
- Volovat C, Bondarenko IM, Gladkov OA et al. Phase III randomized double-blind placebo-controlled, multicentre study of lipegfilgrastim in patients with non-small lung cancers receiving myelosuppressive therapy. SpringerPlus 2015;4:316

Prophylaxis of Infections

rarely applicable to Patients with Solid Tumors (e.g. BC)

ASCO Practice Guideline „Antimicrobial Prophylaxis...“ 2013

	Oxford / LoE	/ GR	AGO
➢ Avoidance of highly infection-risking behaviour or situations	5	D	+
➢ Prophylactic treatment in low risk patients	1a	B	-
➢ Prophylactic treatment in high risk* patients (e.g. according to NCCN Guidelines) with			
➢ Antibiotics	1a	A	++
➢ Anti-fungal agents (triazole)	1a	B	+/-
➢ Virostatics in solid tumors	5	D	-
➢ Granulocyte colony-stimulating factors	1a	A	++

*** High risk: estimated duration of neutropenia < 100/µl ≤ 7d**

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Further Information

References

Mucositis Prevention

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

Multidisciplinary S 3 guidelines of the AWMF (Reg.-Nr. 032-054OL):
„Supportive Therapie bei onkologischen PatientInnen - interdisziplinäre Querschnittsleitlinie“, released 11.11.2016

Oxford / AGO
LoE / GR

- **Standardised mouth hygiene for prophylaxis of oral mucositis should be adhered to by all age groups and during all cancer-related therapies with any risk for oral mucositis.**

2b ++

This entails:

1)patient:

- **Regular mouth washs (H_2O, NaCl)**
- **Soft tooth brushs**
- **Interdental care: flossing or using interdental brush**
- **Avoidance of alcohol, tabac, hot food, sour food**
- **Regular screening for lesions**

2) Risk adjusted prophylaxis by dentician

3) Continuous clinical control

Mucositis

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

- **Desinfecting / antiphlogistic measures**:
  Mouth rinsing with infusions of chamomile or salvia, extracts of chamomile, etheric oils, polyvidon-iodine, hexetidine. Local therapy with crystal violet solution 0.5% or tinctura myrrhei, H. mometasonfuroate + propylene glycol
- **Mucosa protecting measures (during / after application of chemotherapy):**
  Sucking ice cubes (especially from pineapple juice) during 5-fluorouracile- or HD-melphalane. Calcium folinate (Leucovorin-mouth gel®) every 4–6 hrs for HD-methotrexate: do not start earlier than 24 hours after end of MTX-Infusion (otherwise potential loss of efficacy of MTX!). Dexpanthenole (Panthenol®-Solution. 5%) mouth rinsing.
- **Local antimycotic treatment**:
  Amphotericine B, nystatine, fluconazole
- **Local antiviral treatment**
  Aminoquinuride / tetracaine-HCl , Aciclovir®
- **Local anaesthesia:**
  Benzocaine, Doxepin 0,5% p.o.
- **Pain Therapy:** Opioids if indicated

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Version 2017.1

Paravasates with Potentially Necrotising Substances (Anthracycline, Taxane, Vinorelbin)

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Version 2017.1

	Oxford / LoE / GR	AGO	
➢ **Dexrazoxane for treatment of Anthracyclin-Paravasates (exception: liposomal A)**	2b	B	++
➢ **Hyaluronic Acid for treatment of Taxan/Vinorelbin-Paravasates**	3b	D	++

Paravasation Dexrazoxane/Hyaluronic Acid

Dexrazoxane for treatment of anthracyclines paravasates

Day 1: 1000 mg/m² (max. 2000 mg), IV 1–2 hrs

Day 2: 1000 mg/m² (max. 2000 mg), IV 1–2 hrs

Day 3: 500 mg/m² (max. 1000 mg), IV 1–2 hrs

Otherwise or if treatment with dexrazoxane is not indicated, following measures are recommended:

1. **Local cooling: ice packs for 15 min every 6 hrs, for at least 3 days, alternatively: 24 h continuous ice cooling**
2. **Local application (with swab) of dimethylsulfoxid 99% (DMSO) every 3-4 hours for at least 3 days (better 14 days), allow it to dry on air. The interval may be extended to 6 hours from day 4 onward.**

Hyaluronic Acid in case of Taxan/Vinorelbin Paravasates:

- **1-10 Amp a 150 IU**
- **1 ml dissolvent (z.B. NaCl 0.9%)**
- **Local anaesthesia**
- **No thermotherapy after taxanes**
- **Dry warmth 4 x daily 20 min during vincaalkaloids**

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References

Antiemetic Therapy

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

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Version 2017.1

	Oxford / LoE	GR	AGO
➢ After assessment of emetic potential of chemotherapy protocol	5	D	++
➢ Neurokinin-1-receptor-antagonists	1b	A	++
➢ Dexamethasone	1a	A	++
➢ 5-HT_3-antagonists	1b	A	++
➢ Fixed antiemetic combination therapy	1b	A	++
➢ Metoclopramide	3b	C	+

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Further Information

References

Supportive Therapy
Antiemetics

Guidelines Breast
Version 2017.1

Hesketh, Paul J, Bohlke K, Lyman GH et al. Antiemetics: American society of clinical oncology focused guideline update. J Clin Oncol 2016;34:381-6

Jordan K, Jahn F, Aapro M. Recent developments in the prevention of chemotherapy induced nausea and vomiting. Ann Oncol 2015;26:1081-90.

Hesketh PJ, Aaapro M, Jordan K et al. A review of NEPA, a novel fixed antiemetic combination with the potential for enhancing guideline adherence and improving control of chemotherapy-induced nausea and vomiting. Biomed Res Int 2015;65:1879

Schwartzberg LS, Rugo HS, Aapro M. New and emerging therapeutic options for the management of chemotherapy-induced nausea and vomiting Clin Adv Hematol Oncol 2015;15(3 Suppl. 3):3-13

Jordan K, Schaffrath F, Jahn F et al. Neuropharmacology and management of chemotherapy-induced nausea and vomiting in patients with breast cancer. Breast Care 2014;9:246-53

Supportive Therapy Antiemetics

Substance group	Substance	Dosage	Side effects	Potential
Serotoninantagonists	Ondansetron Tropisetron Granisetron Palonosetron	8 mg i.v., 2 x 4-8 mg p.o, transdermal 5 mg i.v., 5 mg p.o. 1-3 mg i.v. 0, 25 mg i.v.	Headaches. Diarrhea, flush symptome, increase of transaminases, intestinal atony at high dosages.	Very high
NK1-Antagonists	Aprepitant Fosaprepitant	125 mg d1, 80 mg d 2-3 p.o. 150 mg d1 i.v.	Cytochrom-P-450-activation with dose reduction of Dxamethasone (2 x 8 mg). Do not combine with Astemizol, Terfenadin, Cisaprid	Very high
Dopaminantagonists/ substituted Benzamids	Metoclopramid Alizaprid	up to 120 mg/24h as a steady infusion or as drops up tp 300 mg i.v. or p.o./24 h (6 Amp. od. 6 tbl.)	Dyskinesia (Antidot:Biperiden) Anxiousness, Depression, Diarrhea	High
Phenothiazins/ Butyrophenons	Haloperidol	1-3 mg 4 x/d	Sedation, Cramps, transient increase of biochemical liver function values	Moderate
Corticosteroids	Dexamethason Prednisolon	8-20 mg i.v. 1-3 x/d 100-250 mg i.v. 1-3 x/d	Extreme blood sugar values, psychotic reactions, flush syndrome, Hypertension	Moderate
NEPA (Netupitant and Palonosetron)	fixed combinations (oral)	NE 300 mg PA 0,5 mg		Very high

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Version 2017.1

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Further Information

References

Analgesia

(Deutsche Gesellschaft für Schmerztherapie Praxisleitlinie Tumorschmerz 2014 www.dgs-praxisleitlinien.de)

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- **Non-opioids; WHO Step 1**
  Diclofenac resinate, ibuprofene and / or metamizole, paracetamole
- **Mild opioids; WHO Step 2**
  Tramadol (preferentially „retard“-formulations)
  or tilidine / naloxone (also as „retard“-formulations)
- **Strong opioids; WHO Step 3**
  Morphine, buprenorphine (sublingual or transdermal), fentanyle (transdermal), hydromorphone, oxycodone, as a back-up levomethadone. The dose of opioids should be titrated step by step according to the analgetic effect.
- **Additional drugs – „adjuvants“**
  Gabapentine, pregabaline, carbamazepine, amitriptyline, bisphosphonats

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References

Diarrhea

- **Adsorbent agents**
  - Carbo medicinalis*; caoline / pectine, Al-Mg-silicate hydrate*
- **Analgetics, opioids**
  - Loperamide; c*odeine, morphine IV, tinctura opii, butylscopolamine*
- **Colitis pseudomembranosa**
  - Metronidazols *or (if not effective) vancomycine*

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Constipation
Important Side Effect of Opioid Treatment

- **Bulging agents**
  - Psylium, flaxseed (shredded)
- **Osmotic laxatives**
  - Macrogol > Lactulose (Cochrane review **LoE 1a, AGO +**)
  - Oral radio-opaque material: ultima ratio e.g. sodium amidotrizoate
  - Sorbite
- **Motility stimulating laxatives**
  - Sennae, Ricinus, Bisacodyl, sodium-picosulfate
- **Emollients** (Internal lubricants e.g. paraffin)
- **Opioid-receptor-antagonists (in opioid-related constipation)**
  - Methylnaltrexone

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Further Information

References

Skin toxicities

Multidisciplinary S 3 guidelines of the AWMF (Reg.-Nr. 032-054OL):
„Supportive Therapie bei onkologischen PatientInnen - interdisziplinäre Querschnittsleitlinie“, released 11.11.2016

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	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

Scalp Cooling Alopecia Prevention trial (SCALP)

J Clin Oncol 34, 2016 (suppl; abstr TPS10144) Nangia JR, Wang T, Niravath PA et.: Scalp Cooling Alopecia Prevention trial (SCALP) for patients with early stage breast cancer

<u>Design</u>
Randomized trial, scalp cooling device vs. control

Assessed for: alopecia, quality of life, device safety

<u>Results</u>
Primary Outcome: hair preservation

Cooling: 50.5 % success vs. 49.5 % failure
Non-cooling: 0 % success vs. 100 % failure

Fisher's exact test $p < 0.001$

Prevention of CIPN

(chemotherapy induced peripheral polyneuropathia)
Multidisciplinary S 3 guidelines of the AWMF (Reg.-Nr. 032-054OL):
„Supportive Therapie bei onkologischen PatientInnen - interdisziplinäre Querschnittsleitlinie“, released 11.11.2016

	Oxford / LoE / GR	AGO
➢ Physical activity reduces the functional losses	5	+
➢ There is no effective prevention of CIPN	1b	--
➢ Alpha-liponic acid	1b	--
➢ Amifostine	1a	--
➢ Carbamazepine	1b	--
➢ Vit E	1a	--
➢ L-Carnitine	1b	--

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Therapy of CIPN

Multidisciplinary S 3 guidelines of the AWMF (Reg.-Nr. 032-054OL):
„Supportive Therapie bei onkologischen PatientInnen - interdisziplinäre Querschnittsleitlinie“, released 11.11.2016

	Oxford / LoE / GR	AGO
➢ Physical Therapy	5	+
➢ Duloxetine for pain induced by CIPN	1b	+
➢ Gabapentine	1b	+
➢ Amitryptiline	1b	+
➢ Venlafaxine	5	+
➢ Pregabaline	5	+
➢ Lamotrigine	1b	-
➢ Opioids for treatment of CIPN-induced pain	5	+
➢ Capsaicine / Lidocaine locally	5	+
➢ Menthol locally (1%)	5	+
➢ Baclofene		

Palliative Care

- "…expert consensus that **combined standard oncology care and palliative care** should be **considered early in the course of illness** for **any patient with metastatic cancer and/or high symptom burden**."[1]

- "Palliative care should be **initiated by the primary oncology team** and augmented by **collaboration** with an interdisciplinary team of palliative care experts."[2]

- "Expert **palliative care**, including effective control of pain and other symptoms, **should be a priority**."[3]

[1] Smith et al, J Clin Oncol 30 880-887, 2012
[2] Levy et al, J Natl Compr Canc Netw 10:1284-1309, 2012
[3] Cardoso et al, Breast 21:242-252, 2012

Supportive Care (2/28)

No further information

No references

Guideline spectrum (3/28)

No further information

No references

Erythropoesis-Stimulating Agents (ESAs) (4/28)

No further information

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Phase III Study of Epoetin Alfa Versues Best Standard of Care ….(5/28)

No further information

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Practical use of ESAs (6/28)

No further information

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Relevant Guidelines

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Cancer- and Chemotherapy-Induced Anemia. Version 2.2017

Relevant Guidelines (7/28)

No further information

No references

Granulocyte Colony-stimulating Factors (8/28)

No further information

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No further information

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No further information

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No further information

No references

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No further information

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No further information

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No further information

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No further information

No references

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No further information

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