Supportive Care
Supportive Care

- **Version 2002:**
  - Diel

- **Versions 2003–2016:**

- **Version 2017:**
  - Möbus / Nitz
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)

<table>
<thead>
<tr>
<th>Oxford / LoE / AGO</th>
<th>AGO</th>
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<td>&lt;a&gt;1a&lt;/a&gt; B</td>
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<td>&lt;a&gt;1a&lt;/a&gt; A +</td>
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<td>&lt;a&gt;1a&lt;/a&gt; A</td>
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</table>

- **Indicated in asymptomatic anaemia**
- **Therapy and secondary prophylaxis in CIA**
  - In the adjuvant setting
  - In the neoadjuvant/metastatic setting
- In dose-dense / dose-escalated CT (iddETC)
- Treatment start at Hb-levels < 10 g/dL
- Target Hb 11–12 g/dL
- Improvement of outcome (DFS, OS)
- Risk of thromboembolic events is increased by use of ESAs
Phase III Study of Epoetin Alfa Versus Best Standard of Care in Anemia Patients with Metastatic Breast Cancer

N=2,098 Pat., Hb <11g/dl; non inferiority study.  
Prespecified upper non inferiority margin = 1.15

<table>
<thead>
<tr>
<th></th>
<th>PFS (median)</th>
<th>OS (median)</th>
<th>ORR</th>
<th>RBC transfusions</th>
<th>TVE</th>
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<tr>
<td>Epo</td>
<td>Invest.* 7,4 Mon</td>
<td>IRC** 7,6 Mon</td>
<td>17,2 Mon</td>
<td>50%</td>
<td>5,8%</td>
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<tr>
<td>BSC</td>
<td>7,4 Mon.</td>
<td>7,6 Mon.</td>
<td>17,4 Mon</td>
<td>51%</td>
<td>11,4%</td>
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</table>

HR: 1,09  
HR: 1,02  
HR: 1,06  
OR: 0,95  
p<.001  
p=.04

Upper Cl: 1,20  
Upper Cl: 1,146

* Investigator determined  
**Independent review committee
Practical Use of ESAs

- 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 β: 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
Relevant Guidelines


Granulocyte Colony-stimulating Factors

- **Primary prophylaxis for expected febrile neutropenia (FNP)**
  - If expected risk for FNP 10–20%  
    - In case of individual risk factors
  - If expected risk for FNP >20% (e.g. DAC, dose-dense CT)

- **Secondary prophylaxis during chemotherapy**  
  (previous FNP or neutropenia grade IV > 7 days)

- **Therapeutic usage for FNP**

- **Start related to chemotherapy and duration**
  - Pegfilgrastim day 2
  - Lipegfilgrastim day 2
  - Filgrastim/Lenograstim from day 2–3 until ANC > 2–3 x 10^9
### 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](http://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)

<table>
<thead>
<tr>
<th>Action</th>
<th>Oxford</th>
<th>LoE</th>
<th>AGO</th>
<th>GR</th>
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<td>Clinical examination</td>
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<td>D</td>
<td>++</td>
<td></td>
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<tr>
<td>Daily evaluation</td>
<td>5</td>
<td>D</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Hospitalization of high risk patients</td>
<td>1b</td>
<td>A</td>
<td>++</td>
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</tr>
<tr>
<td>Homecare in low risk patients</td>
<td>1b</td>
<td>A</td>
<td>+</td>
<td></td>
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<tr>
<td>Differential blood count</td>
<td>5</td>
<td>D</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Blood cultures</td>
<td>5</td>
<td>D</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Imaging of lungs</td>
<td>3</td>
<td>C</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Immediate initial empiric antibiotic therapy</td>
<td>1a</td>
<td>A</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Empiric antifungal therapy 4–7d</td>
<td>1b</td>
<td>A</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>in case of failure of antibiotic therapy</td>
<td>1b</td>
<td>A</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>G-CSF for treatment (not prophylactic)</td>
<td>2b</td>
<td>B</td>
<td>+/-</td>
<td></td>
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</tbody>
</table>
Empirical Antibiotic Therapy

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.
Step 1: Assess frequency of FN associated with the planned chemotherapy regimen

- FN risk ≥20%
- FN risk 10-20%
- FN risk <10%

Step 2: Assess factors that may increase the risk of FN:

- **High risk:** Age >65 years
- **Increased risk:**
  - Advanced disease
  - History of prior FN
  - No antibiotic prophylaxis
- **Other Factors:**
  - Poor performance (ECOG > 1)
  - Female gender
  - Haemoglobin <12 g/dL
  - Liver, renal or cardiovascular disease
  - Nutritional status

Step 3: Define the patient’s overall FN risk for planned chemotherapy regimen

- Overall FN risk ≥20%
- Overall FN risk <20%

**Prophylactic G-CSF recommended**

**G-CSF prophylaxis not indicated**
Relevant Guidelines

Prophylaxis of Infections
rarely applicable to Patients with Solid Tumors (e.g. BC)
ASCO Practice Guideline „Antimicrobial Prophylaxis...“ 2013

- Avoidance of highly infection-risking behaviour or situations [5D+]
- Prophylactic treatment in low risk patients [1aB-]
- Prophylactic treatment in high risk* patients (e.g. according to NCCN Guidelines) with
  - Antibiotics [1aA++]
  - Anti-fungal agents (triazole) [1aB+-/]
  - Virostatics in solid tumors [5D-]
  - Granulocyte colony-stimulating factors [1aA++]

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

This entails:

1) patient:
   - Regular mouth washes (H₂O, NaCl)
   - Soft tooth brushes
   - Interdental care: flossing or using interdental brush
   - Avoidance of alcohol, tabac, hot food, sour food
   - Regular screening for lesions

2) Risk adjusted prophylaxis by dentist

3) Continuous clinical control

Oxford / AGO
LoE / GR

2b ++
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
Paravasates with Potentially Necrotising Substances
(Anthracycline, Taxane, Vinorelbin)

- **Dexrazoxane** for treatment of Anthracyclin-Paravasates
  (exception: liposomal A)  
  Oxford / AGO LoE / GR  
  2b  B  ++

- **Hyaluronic Acid** for treatment of Taxan/Vinorelbin-Paravasates  
  Oxford / AGO LoE / GR  
  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
### Antiemetic Therapy

After assessment of emetic potential of chemotherapy protocol

<table>
<thead>
<tr>
<th>Drug</th>
<th>Oxford LoE</th>
<th>AGO LoE</th>
<th>AGO GR</th>
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<tbody>
<tr>
<td>Neurokinin-1-receptor-antagonists</td>
<td>1b</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>1a</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>5-HT3-antagonists</td>
<td>1b</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>Fixed antiemetic combination therapy</td>
<td>1b</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>3b</td>
<td>C</td>
<td>+</td>
</tr>
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</table>
Supportive Therapy
Antiemetics

Hesketh, Paul J, Bohlke K, Lyman GH et al.


## Supportive Therapy

### Antiemetics

<table>
<thead>
<tr>
<th>Substance group</th>
<th>Substance</th>
<th>Dosage</th>
<th>Side effects</th>
<th>Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotonin antagonists</td>
<td>Ondansetron</td>
<td>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.</td>
<td>Headaches, Diarrhea, flush symptoms, increase of transaminases, intestinal atony at high dosages.</td>
<td>Very high</td>
</tr>
<tr>
<td></td>
<td>Tropisetron</td>
<td>5 mg i.v.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Granisetron</td>
<td>1-3 mg i.v.</td>
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<tr>
<td></td>
<td>Palonosetron</td>
<td>0, 25 mg i.v.</td>
<td></td>
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</tr>
<tr>
<td>NK1-Antagonists</td>
<td>Aprepitant</td>
<td>125 mg d1, 80 mg d 2-3 p.o.</td>
<td>Cytochrom-P-450-activation with dose reduction of Dexamethasone (2 x 8 mg). Do not combine with Astemizol, Terfenadin, Cisaprid</td>
<td>Very high</td>
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<tr>
<td></td>
<td>Fosaprepitant</td>
<td>150 mg d1 i.v.</td>
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<tr>
<td>Dopaminantagonists/substituted Benzamids</td>
<td>Metoclopramide</td>
<td>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.)</td>
<td>Dyskinesia (Antidot: Biperiden) Anxiousness, Depression, Diarrhea</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>Alizaprid</td>
<td>up tp 300 mg i.v. or p.o./24 h (6 Amp. od. 6 tbl.)</td>
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</tr>
<tr>
<td>Phenothiazins/Butyrophenons</td>
<td>Haloperidol</td>
<td>1-3 mg 4 x/d</td>
<td>Sedation, Cramps, transient increase of biochemical liver function values</td>
<td>Moderate</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Dexamethason</td>
<td>8-20 mg i.v. 1-3 x/d</td>
<td>Extreme blood sugar values, psychotic reactions, flush syndrome, Hypertension</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Prednisolon</td>
<td>100-250 mg i.v. 1-3 x/d</td>
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<td></td>
</tr>
<tr>
<td>NEPA (Netupitant and Palonosetron)</td>
<td>fixed combinations (oral)</td>
<td>NE 300 mg PA 0,5 mg</td>
<td></td>
<td>Very high</td>
</tr>
</tbody>
</table>
Analgesia
(Deutsche Gesellschaft für Schmerztherapie Praxisleitlinie
Tumorschmerz 2014 www.dgs-praxisleitlinien.de)

- **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), fentanyl (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
Diarrhea

- Adsorbent agents
  - Carbo medicinalis; caoline / pectine, Al-Mg-silicate hydrate

- Analgetics, opioids
  - Loperamide; codeine, morphine IV, tinctura opii, butylscopolamine

- Colitis pseudomembranosa
  - Metronidazols or (if not effective) vancomycine
Constipation

Important Side Effect of Opioid Treatment

- **Bulging agents**
  - Psyllium, 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
Avoidance of chemotherapy-induced alopecia 1b +/− by cooling the patient’s scalp*

- Prophylaxis of hand-foot-syndrome 1b + using urea containing lotions (5-10%)

- Prophylaxis of nail changes and hand-foot-syndrome 2b + by cooling hands during application of docetaxel

*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

**Design**
Randomized trial, scalp cooling device vs. control

Assessed for: alopecia, quality of life, device safety

**Results**
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

- Physical activity reduces the functional losses
- There is no effective prevention of CIPN
  - Alpha-liponic acid
  - Amifostine
  - Carbamazepine
  - Vit E
  - L-Carnitine
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

- Physical Therapy
- Duloxetine for pain induced by CIPN
- Gabapentine
- Amitryptiline
- Venlafaxine
- Pregabaline
- Lamotrigine
- Opioids for treatment of CIPN-induced pain
- Capsaicine / Lidocaine locally
- Menthol locally (1%)
- Baclofene

<table>
<thead>
<tr>
<th>Treatment</th>
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<th>AGO LoE</th>
<th>AGO GR</th>
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</thead>
<tbody>
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<td>Physical Therapy</td>
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<td>+</td>
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</tr>
<tr>
<td>Duloxetine for pain induced by CIPN</td>
<td>1b</td>
<td>+</td>
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<tr>
<td>Gabapentine</td>
<td>1b</td>
<td>+</td>
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<tr>
<td>Amitryptiline</td>
<td>1b</td>
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<td>Venlafaxine</td>
<td>5</td>
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<td>Pregabaline</td>
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<tr>
<td>Opioids for treatment of CIPN-induced pain</td>
<td>5</td>
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<td>Capsaicine / Lidocaine locally</td>
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<td>Menthol locally (1%)</td>
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<td>+</td>
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<tr>
<td>Baclofene</td>
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</table>
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
Supportive Care (2/28)

No further information

No references
Guideline spectrum (3/28)

No further information

No references
Erythropoiesis-Stimulating Agents (ESAs) (4/28)

No further information

References:


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

No further information

References:

Practical use of ESAs (6/28)

No further information

References:


Relevant Guidelines

Relevant Guidelines (7/28)

No further information

No references
Granulocyte Colony-stimulating Factors (8/28)

No further information

References:


Management of Febrile Neutropenia (9/28)

No further information

References:

Empirical Antibiotic Therapy (10/28)

No further information

No references
EORTC and ASCO G-CSF Guideline-Based FN Risk Assessment (11/28)

No further information

No references
Relevant Guidelines (12/28)

No further information

No references
Prophylaxis of Infections (13/28)

No further information

No references
Mukositis Prevention (14/28)

No further information

No references
Mucositis (15/28)

No further information

No references
**Paravasates with Potentially Necrotising Substances (Anthracycline, Taxane, Vinorelbin) (16/28)**

No further information

**References:**


**Relevant practice guideline:**

Paravasation Dexrazoxane/Hyaluronic Acid (17/28)

No further information

No references
Antiemetic Therapy (18/28)

No further information

References:

1. Keith B. : Systematic review of the clinical effect of glucocorticoids on nonhematologic malignancy BMC Cancer (2008);8:84


Supportive Therapy Antiemetics (19/28)

No further information

No references
Supportive Therapy Antiemetics (20/28)

No further information

No references
Analgesia (21/28)

No further information

References:

Relevant practice guideline:
Deutsche Gesellschaft zum Studium des Schmerzes, www.dgss.org
Diarrhea (22/28)

No further information

No references
Constipation- Important Side Effect of Opioid Treatment (23/28)

No further information

No references
Skin toxicities (24/28)

No further information

References:

Relevant practice guideline:

Multidisciplinary S 3 guidelines of the AWMF (Reg.-Nr. 032-054OL):
„Supportive Therapie bei onkologischen PatientInnen - interdisziplinäre Querschnittsleitlinie“, released 11.11.2016
Scalp Cooling Alopecia Prevention trial (SCALP) (25/28)

No further information

References:

1. 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
Prevention of CIPN, (chemotherapy induced peripheral polyneuropathia) (26/28)

No further information

References:


Relevant practice guideline:

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

1. www.mascc.org
2. Keith B.: Systematic review of the clinical effect of glycocorticoids on nonhematologic malignancy BMC Cancer (2008);8:84
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Relevant practice guideline:

No further information

No references