Supportive Care
Supportive Care

- **Version 2002:**
  Diehl

- **Versions 2003–2013:**

- **Version 2014:**
  Schmidt / Möbus
Guideline Spectrum

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

We try to quote these guidelines wherever appropriate, but underline that the listings of relevant guidelines do not claim to be complete. The listing is clearly biased towards German and English language.

Special emphasis is put on aspects concerning breast cancer patients.

In the German environment, special interest is earnt by the publications of the „Arbeitsgem. Supportive Maßnahmen in der Onkologie, Rehabilitation und Sozialmedizin der DKG: http://www.onkosupport.de“

In preparation: multidisciplinary guidelines of the AWMF:

„Supportive Therapie bei onkologischen Patientinnen - interdisziplinäre Querschnittsleitlinie“, announced 1.7.2012, planned release: 30.6.2015

„Palliativmedizin“, announced 03.12.2010, planned release 31.03.2014
Erythropoiesis-stimulating agents (ESAs)

- Indicated in asymptomatic anaemia
  - In dose-dense / dose-escalated CT (iddETC)

- Indicated in symptomatic anaemia
  - In the adjuvant setting
  - In the neoadjuvant/metastatic setting

- Treatment and secondary prophylaxis of chemotherapy induced anemia (CIA)
- Improvement of outcome (DFS, OS)
- Treatment start at Hb-levels approaching < 10 g/dL
- Target Hb 11–12 g/dL
- Thromboembolic events are increased with ESAs

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Practical Use of ESAs

- Epoetin α and Darbepoetin are equieffective

**Dose:**
- Epoetin α: 150 IU/kg 3 x weekly s.c. or 40,000 IU 1 x /week s.c.
- Epoetin α: 80,000 IU q2w s.c. or 120,000 IU q3w s.c.
- Darbepoetin: 2,25 µg/kg s.c. weekly
- Darbepoetin: 500 µg s.c. q3w

- Hb measurements weekly
  - Dose reduction at Hb-increase > 1g/dl within 2 weeks
  - Dose increase at Hb-increase < 1g/dl within 4-6 weeks

- In case of FID give IV iron supplementation
- p.o. iron supplementation
- STOP ESA-treatment in case of missing increases of Hb-levels after 9 weeks

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**Oxford / AGO LoE / GR**

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Relevant Guidelines


Prophylaxis of Infections

NB Rarely Applicable to Patients with Solid Tumors (e.g. BC)

ASCO Practice Guideline „Antimicrobial Prophylaxis...“ 2013

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

* High risk definition: estimated duration of neutropenia \(< 100/\mu l \geq 7d\)
Relevant Guidelines

Mucositis


- **Desinfecting / antiphlogistic measures:**
  Mouth rinsing with infusions of camomile or salvia, extracts of camomile, 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-Mundgel®) 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 PO
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 10⁹
Relevant Guidelines

Management of Febrile Neutropenia


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)

- Clinical examination
- Daily evaluation
- Hospitalization of high risk patients
- Homecare in low risk patients
- Differential blood count
- Blood cultures
- Imaging of lungs
- Immediate initial empiric antibiotic therapy
- Empiric antifungal therapy 4–7d in case of failure of antibiotic therapy
- G-CSF for treatment (not prophylactic)

Oxford / AGO LoE / GR

- 5 D ++
- 5 D ++
- 1b A ++
- 1b A +
- 5 D ++
- 5 D ++
- 3 C ++
- 1a A ++
- 1b A ++
- 2b B +/-
Calculated Antibiotic Therapy in FN

Recommendations need to be regularly updated according to the changes in microbial sensitivity and resistance towards antiinfective treatments.

Arbeitsgemeinschaft Infektionen in der Hämatologie und Onkologie (AGIHO) der Deutschen Gesellschaft für Hämatologie und Onkologie e.V. (DGHO) regularly issues such recommendations in German.
## Dexrazoxane

| Treatment of anthracycline extravasation | 2b | B | + |
| In combination with anthracyclines for cardiac protection | 1a | B | +/- |
| In cardiac risk patients | 1b | B | + |
| Dexrazoxane | 5 | D | ++ |
| Consider alternative regimens (anthracycline-free, liposomal) |  |  |  |

http://www.onkosupport.de/e974/e2538/e3782/e3494/ASORS_AV_Paravasate-Guidelines_04-2010.pdf

Oxford / AGO LoE / GR
Paravasation
Dexrazoxane

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.
After assessment of emetic potential of chemotherapy protocol

- Neurokinin-1-receptor-antagonists
- Dexamethasone
- 5-HT$_3$-antagonists
- Metoclopramide

Oxford / AGO LoE / GR

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<td>Metoclopramide</td>
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MASCC/ESMO Antiemetic Guideline 2011

Multinational Association of Supportive Care in Cancer

Organisation und Vorstand:
Richard J. Gralla, MD
Fausto Roila, MD
Maurizio Tonato, MD
Jørn Herrstedt, MD
## Supportive Therapy

### Antiemetics

<table>
<thead>
<tr>
<th>Wirkstoffgruppe</th>
<th>Substanz</th>
<th>Dosierung</th>
<th>Nebenwirkungen</th>
<th>Potenzial</th>
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<tr>
<td>Serotoninantagonisten</td>
<td>Ondansetron</td>
<td>8 mg i.v., 2 x 4-8 mg p.o.</td>
<td>Kopfschmerzen, Diarrhoe, Flushsymptomatik</td>
<td>sehr hoch</td>
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<tr>
<td></td>
<td>Tropisetron</td>
<td>5 mg i.v., 5 mg p.o.</td>
<td>Transaminasenanstieg</td>
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<tr>
<td></td>
<td>Gransetron</td>
<td>1-3 mg i.v.</td>
<td>Darmatonie in hoher Dosierung</td>
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<td></td>
<td>Palonosetron</td>
<td>0, 25 mg i.v.</td>
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<td>NK 1-Antagonisten</td>
<td>Aprepitant</td>
<td>125 mg d1,</td>
<td>Cytochrom-P-450-Aktivierung mit Dosisreduktion von Dexamethason (2 x 8 mg). Keine Kombination mit Astemizol, Terfenadin, Cisaprid</td>
<td>sehr hoch</td>
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<td>Fosaprepitant</td>
<td>150 mg d1 i.v.</td>
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<td>Dopaminantagonisten/substituierte Benzamide</td>
<td>Metoclopramid</td>
<td>bis zu 120 mg/24h als Dauerinfusion od. als Tropfen</td>
<td>Dyskinesien (Antidot: Biperiden)</td>
<td>hoch</td>
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<td>Alizaprid</td>
<td>bis zu 300 mg i.v. oder p.o./24 h (6 Amp. od. 6 Tbl.)</td>
<td>Angstreaktion, Depressionen, Diarrhoe</td>
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<td>Phenothiazine/Butyrophenone</td>
<td>Haloperidol</td>
<td>1-3 mg 4 x/d</td>
<td>Sedation, Senkung der Krampfschwelle, transiente Leberwerterhöhung</td>
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<tr>
<td>Corticosteroide</td>
<td>Dexamethason</td>
<td>8-20 mg i.v. 1-3 x/d</td>
<td>Blutzuckerentgleisung, psychotische Reaktionen, Flush, Blutdruckanstieg</td>
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<td>Prednisolon</td>
<td>100-250 mg i.v. 1-3 x/d</td>
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<td>Benzodiazepine</td>
<td>Diazepam</td>
<td>bis zu 20 mg/d</td>
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<td>Lorazepam</td>
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<td>Antihistaminika</td>
<td>Dimenhydrinat</td>
<td>bis zu 3 x 50 mg/d</td>
<td>Sedation, Mundtrockenheit</td>
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Analgesia
(See Specific Guidelines for Analgesia www.dgss.org)

- **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 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) vancomycin
Constipation
Important Side Effect of Opioid Treatment

- **Swelling 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
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 (2/22)

No further information

No references
**Guideline spectrum (3/22)**

*Further information:*

Specific national and international guidelines deal with various aspects of evidence-based supportive therapy of cancer patients. We try to quote these guidelines wherever appropriate, but underline that the listings of relevant guidelines do not claim to be complete. The listing is clearly biased towards German and English language. Special emphasis is put on aspects concerning breast cancer patients. In the German environment, special interest is earned by the publications of Arbeitsgem. Supportive Maßnahmen in der Onkologie, Rehabilitation und Sozialmedizin der DKG: [http://www.onkosupport.de](http://www.onkosupport.de)


*No references*
**Erythropoiesis-Stimulating Agents (ESAs) (4/22)**

*Further information:*

Prior to 2007, the erythropoiesis-stimulating agents (ESAs) epoetin alfa and darbepoetin alfa were indicated for use in chemotherapy-induced anemia to achieve target hemoglobin (Hb) levels of approximately 12 grams per deciliter (gm per dL), and treatment was to be withheld if Hb exceeded 13 gm per dL. In March 2007, the FDA changed the labeling of the ESAs to add boxed warnings, updated in November 2007, to include the following key points: (a) ESAs should be used only to treat anemia that occurs in patients with cancer while they are undergoing chemotherapy; (b) treatment with ESAs should be stopped when chemotherapy ends; and (c) dosing ESAs to an Hb target of 12 gm per dL or greater has resulted in more rapid cancer progression or shortened overall survival in patients with breast, head and neck, lymphoid, cervical, and non-small cell lung malignancies. In January 2008, the FDA specified that the increased risk of more rapid tumor growth or shortened survival was associated with ESAs when "administered in an attempt to achieve a Hb level of 12 gm per dL or greater, although many patients did not reach that level." A new black-box warning regarding this association was added to the labels of the ESAs in March 2008, and the FDA mandated further label changes on July 30, 2008, that ESA therapy should not be initiated in patients receiving chemotherapy at Hb levels of 10 gm per dL or higher.

**OBJECTIVE:** To (a) assess the prevalence and predictors of ESA administrations at Hb levels above 12 gm per dL among patients with a diagnosis of solid or hematologic cancer or myelodysplastic syndrome who began their first regimen of conventional myelosuppressive chemotherapy between 2002 and 2006, and (b) describe patterns of ESA treatment subsequent to the first ESA administration at Hb above 12 gm per dL.

In 2012 a Cochrane review was published by Tonia et al., extracting data from a total of 91 trials with 20,102 participants to perform a systematic review, concluding that ESAs reduce the need for red blood cell transfusions but increase the risk for thromboembolic events and deaths. There is suggestive evidence that ESAs may improve QoL. Whether and how ESAs affects tumour control remains uncertain. The increased risk of death and thromboembolic events should be balanced against the potential benefits of ESA treatment taking into account each patient’s clinical circumstances and preferences. More data are needed for the effect of these drugs on quality of life and tumour progression. Further research is needed to clarify cellular and molecular mechanisms and pathways of the effects of ESAs on thrombogenesis and their potential effects on tumour growth.
References:


Further references:

Statement: An increased mortality and tumor progression by the use of ESF can not be safely ruled out

levels with epoetin alfa in mainly nonanemic patients with metastatic breast cancer receiving first-line chemotherapy: a survival study, J Clin Oncol. 2005 Sep 1;23(25):5960-72

Relevant Guidelines:

American society of clinical oncology/american society of hematology clinical practice guideline update on the use of epoetin and darbepoetin in adult patients with cancer.
Rizzo JD, Brouwers M, Hurley P, Seidenfeld J, Somerfield MR, Temin S.


Rodgers GM: Cancer- and chemotherapy-induced anemia. NCCN Clinical Practice Guidelines in Oncology 2011
Available from: URL: http://www.nccn.org
Practical Use of ESAs (5/22)

Further information:

For practical use refer to relevant practice guidelines
The increased risk of death and thromboembolic events should be balanced against the potential benefits of ESA treatment taking into account each patient’s clinical circumstances and preferences.

References:

Relevant guidelines (6/22)

No further information

References:


Prophylaxis of Infection (7/22)

Further information:

According to relevant guidelines, antibiotic prophylaxis of asymptomatic patients under chemotherapy should be restricted to high risk cases: one selective criterion could be expected duration of neutropenia of greater than 10 days (NCCN). (ASCO absolute neutrophil count < 100/µl > 7 days) N.B.: Standard chemotherapy protocols such as used in breast cancer patients do not regularly justify antibiotic prophylaxis.

The use of oral prophylactic antibiotics in patients with neutropenia is controversial and not recommended by the Australian Consensus Guidelines 2011 Steering Committee because of a lack of evidence showing a reduction in mortality and concerns that such practice promotes antimicrobial resistance. Recent evidence has demonstrated non-significant but consistent, improvement in all-cause mortality when fluoroquinolones (FQs) are used as primary prophylaxis. However, the consensus was that this evidence was not strong enough to recommend prophylaxis.

Engels EA, Lau J, Barza M. Efficacy of quinolone prophylaxis in neutropenic cancer patients: a meta-analysis. J Clin Oncol 1998;16:1179-1187: In a meta-analysis that evaluated 18 trials (N=1408) in which fluoroquinolones were compared to either placebo or TMP/SMX, fluoroquinolone prophylaxis significantly reduced the incidence of Gram-negative infections by about 80% compared with those without prophylaxis (relative risk=0.21; 95% CI, 0.12-0.37), leading to an overall reduction in total infections.

Latest update: in the latest ASCO Guideline on Antimicrobial Prophylaxis and Outpatient Management… (2013) the use of antimicrobial prophylaxis is only recommended for patients expected to have 100 neutrophils/L for 7 days, unless other factors increase risks for complications or mortality to similar levels. The authors clearly state, that chemotherapy for solid tumors rarely leads to the mentioned conditions. An oral fluoroquinolone is preferred for antibacterial prophylaxis and an oral triazole for antifungal prophylaxis. The guideline encourages the use of myeloid growth factor prophylaxis to render antimicrobial prophylaxis unnecessary.
Interventions such as footwear exchange, protected environments, respiratory or surgical masks, neutropenic diet, or nutritional supplements are not recommended because evidence is lacking of clinical benefits to patients from their use.

References:


Relevant Guidelines
Antimicrobial Prophylaxis and Outpatient Management of Fever and Neutropenia in Adults Treated for Malignancy: American Society of Clinical Oncology Clinical Practice Guideline
Christopher R. Flowers, Jerome Seidenfeld, Eric J. Bow, Clare Karten, Charise Gleason, Douglas K. Hawley, Nicole M. Kuderer, Amelia A. Langston, Kieren A. Marr, Kenneth V.I. Rolston, and Scott D. Ramsey
Published Ahead of Print on January 14, 2013 as 10.1200/JCO.2012.45.8661
Relevant guidelines (8/22)

No further information

References

**Mucositis (9/22)**

**Further information:**


Die Pathogenese der Mukositis ist nicht vollständig geklärt. Diagnostik, Therapie und Prophylaxe werden bisher nicht standardisiert durchgeführt und sind hauptsächlich auf die Symptomkontrolle ausgerichtet.“

**References:**

**Relevant Guidelines**

Granulocyte Colony-stimulating Factors (10/22)

**Further information:**

The ability to deliver the planned dose and intensity of chemotherapy (the amount of drug administered/unit of time) is important for tumor control and survival. In clinical practice, neutropenic events are the main limiting factors towards achieving this aim. Furthermore, severe neutropenia accompanied by fever, so called „febrile neutropenia (FN)“, is the most serious manifestation of neutropenia usually requiring hospitalization and intravenous antibiotics. Without stringent management FN is associated with significant morbidity and mortality. The primary use of recombinant granulocyte colony-stimulating factors has reduced the incidence of febrile neutropenia during dose-dense adjuvant/neoadjuvant chemotherapy programs for breast cancer.

In 2012, a Cochrane review sought to assess the effect of prophylactic colony-stimulating factors (CSFs) in reducing the incidence and duration of FN, and all-cause and infection-related mortality during chemotherapy in patients with breast cancer.

The authors concluded that „In patients with breast cancer receiving chemotherapy, CSFs have shown evidence of benefit in the prevention of FN. There is evidence, though less reliable, of a decrease of all-cause mortality during chemotherapy and a reduced need for hospital care. No reliable evidence was found for a reduction of infection-related mortality, a higher dose intensity of chemotherapy with CSFs or diminished rates of severe neutropenia and infections. The majority of adverse events reported from CSF use were bone pain and injection-site reactions but no conclusions could be drawn regarding late-term side effects.“

In a comparative effectiveness study, pegfilgrastim prophylaxis was associated with a reduced risk of neutropenia-related or all-cause hospitalization relative to filgrastim prophylaxis.

A recent study demonstrated in high risk breast cancer that 6 mg lipegfilgrastim, a novel glyco-pegylated granulocyte-colony stimulating factor, was as effective as pegfilgrastim in reducing neutropenia in patients with breast cancer receiving myelosuppressive chemotherapy.
References:


Relevant Guidelines:

ASCO:


NCCN:
* NCCN Guidelines Version 1.2012 Panel Members Myeloid Growth Factors


Stimulation der Granulopoese mit G-CSF
Relevant guidelines (11/22)

No further information

References:

Management of Febrile Neutropenia (12/22)

Further information:

*The most important treatment aspect is to initiate calculated antibiotic treatment as soon as possible, but no later than 2 hours after onset of fever, according to updated guidelines.*

A Cochrane review sought to evaluate the safety and effectiveness of adding colony stimulating factors (CSF) to antibiotic therapy when treating febrile neutropenia caused by cancer chemotherapy. The authors looked for all randomized controlled trials (RCTs) that compare CSF plus antibiotics versus antibiotics alone for the treatment of established febrile neutropenia in adults and children. After inclusion of 13 studies the authors concluded, that „the use of CSF in patients with febrile neutropenia due to cancer chemotherapy does not affect overall mortality, but reduces the amount of time spent in hospital and the neutrophil recovery period. It was not clear whether CSF has an effect on infection-related mortality.“

References:


**Relevant Guidelines:**

**ASCO:**
*Thomas J. Smith (Chair), James Khatcheressian, Gary H. Lyman, Howard Ozer, James O. Armitage, Lodovico Balducci, Charles L. Bennett, Scott B. Cantor, Jeffrey Crawford, Scott J. Cross, George Demetri, Christopher E. Desch, Philip A. Pizzo, Charles A. Schiffer, Lee Schwartzberg, Mark R. Somerfield, George Somlo, James C. Wade, James L. Wade, Rodger J. Winn, Antoinette J. Wozniak, and Antonio C. Wolff*

**NCCN:**
NCCN Guidelines Version 1.2012 Panel Members Myeloid Growth Factors


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: erstellt 04/07)
**Calculated Antibiotic Therapy in FN (13/22)**

*Further information:*

*The most important treatment aspect is to initiate calculated antibiotic treatment as soon as possible, but no later than 2 hours after onset of fever, according to updated guidelines.* Recommendations need to be regularly updated according to the changes in microbial sensitivity and resistance towards antiinfective treatments.

*References:*

*Relevant practice guidelines:*

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: erstellt 04/07)
**Dexrazoxane (14/22)**

**Further information:**

Anthracyclines are among the most active chemotherapeutic agents in cancer treatment. Although infrequent, cumulative dose-dependent cardiotoxicity is nevertheless a significant side effect of this therapy resulting in reduced cardiac reserve or even frank cardiac failure. Although used in several types of malignancy, anthracyclines are most commonly used in breast cancer treatment. Importantly, recent advances have also seen the increasing use of another cardiotoxic agent, the monoclonal antibody trastuzumab, both in the metastatic as well as in the adjuvant breast cancer setting. A great number of studies review and discusses the relationship of cardiotoxicity and anthracycline use, particularly in the breast cancer setting, and explores available treatment options for the anthracycline-treated patients based on evidence from recent Phase III trials.

Dexrazoxane is not recommended for routine use in breast cancer (BC) in adjuvant setting, or metastatic setting with initial doxorubicin-based chemotherapy. Consider use with metastatic BC and other malignancies, for patients who have received more than 300 mg/m\(^2\) doxorubicin who may benefit from continued doxorubicin-containing therapy. Cardiac monitoring should continue in patients receiving doxorubicin.

A Cochrane review investigated Cardioprotective interventions for cancer patients receiving anthracyclines and concluded: “…The nine included studies of dexrazoxane enrolled 1403 patients. The meta-analysis of dexrazoxane showed a statistically significant benefit in favour of dexrazoxane for the occurrence of heart failure (Relative Risk (RR) 0.29, 95% CI 0.20 to 0.41). No evidence was found for a difference in response rate or survival between the dexrazoxane and control group. Only for one adverse effect (abnormal white blood cell count at nadir) a difference in favour of the control group was identified.“

**References:**


**Paravasation Dexrazoxane (15/22)**

*Further information:*

Although indicated and approved for cardioprotection, dexrazoxane has been suggested as being helpful in the case of anthracyclin paravasation. The agent is administered systemically.

*References:*

*Relevant practice guideline*

Zytostatika-induzierte Paravasate - Empfehlungen zu Diagnose, Prophylaxe und Therapie [ PDF-Datei ]
Arbeitsversion der ASORS Paravasate-Guidelines (Stand April 2010)
Maike de Wit, Petra Ortner, Hans-Peter Lipp, Jalid Sehouli, Michael Untch, Markus Ruhnke, Regine Mayer-Steinacker, Carsten Bokemeyer, Karin Jordan
download: http://www.onkosupport.de/e974/e2538/e3782/e3494/ASORS_AV_Paravasate-Guidelines_04-2010.pdf

Witte J, de Wit M.
Prävention, Diagnostik und Therapie der zytostatikaassozierten Paravasation - Was tun wenn’s brennt?
Im Focus Onkologie 2010;6:50-55.
Further information:

Nausea and vomiting are two of the most severe problems for patients treated with chemotherapy. Until the late 1970s, nausea and vomiting induced by chemotherapy was an almost neglected research area. With the introduction of cisplatin, the cytotoxin with the highest emetic potential, research was stimulated and has now resulted in the development of two new classes of antiemetics, the serotonin and neurokinin antagonists. A large number of trials have fine-tuned antiemetic therapy and made evidence-based recommendations possible for the majority of patients receiving chemotherapy. A systematic Review summarizes recommendations from the evidence-based guidelines developed by the Multinational Association of Supportive Care in Cancer (MASCC).

The combination of ondansetron, dexamethasone and aprepitant is able to protect 66–78% of patients from emesis and 48–49% from nausea during the first cycle of cisplatin-based chemotherapy. In a subsequent trial, single-dose intravenous fosaprepitant (150 mg) given with ondansetron and dexamethasone was noninferior to standard 3-day oral aprepitant in preventing CINV during OP and DP.

In women receiving cyclophosphamide/anthracycline-based chemotherapy for breast cancer, the corresponding figures are 76% and 33%. In patients with breast cancer treated with anthracycline plus cyclophosphamide chemotherapy and receiving the same antiemetic prophylaxis for acute emesis, dexamethasone was not superior to aprepitant but instead had similar efficacy and toxicity in preventing delayed emesis.

New antiemetics have been highly successful in the prophylaxis of emesis, but are less effective in the prevention of nausea. There is, therefore, a particular interest in initiating trials to investigate agents with potential anti-nausea effect, such as olanzapine. Guidelines such as the MASCC antiemetic guidelines are only useful if they are continuously updated and implemented in the daily clinic. To encourage implementation, the MASCC guidelines have been translated into several languages, are updated every 6 months (as new data arise), and are always accessible on the MASCC website.

References:

www.mascc.org
Keith B. Systematic review of the clinical effect of glycocorticoids on nonhematologic malignancy BMC Cancer (2008);8:84
Schmoll HJ et al. (2006) Comparison of an aprepitant regimen with a multiple-day ondansetron regimen, both with dexamethasone, for antiemetic efficacy in high-dose cisplatin treatment. Ann Oncol 17: 4112–4119
Massa E, Astara G, Madeddu C, Dessi M, Lopi C, Lepori S, Mantovani G. Palonosetron plus dexamethasone effectively prevents acute and delayed chemotherapy-induced nausea and vomiting following highly or moderately emetogenic chemotherapy in pre-treated patients who have failed to respond to a previous antiemetic treatment: Comparison between elderly and non-elderly patient response. Crit Rev Oncol Hematol. 2008 Aug 23. [Epub ahead of print]


Relevant Guidelines

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

Antiemetische Prophylaxe gemäß MASCC- und ASCO-Guidelines
[ PDF-Datei (auf www.krebgesellschaft.de) ]
Kurzgefasste interdisziplinäre Leitlinie 2008 der Deutschen Krebsgesellschaft, die unter der Verantwortung der ASO bzw. ASORS erstellt wurde.

Supportive Therapie: Antiemetic Guideline MASCC (17/22)

No further information

No references
Supportive Therapie: Antiemetics (18/22)

No further information

No references
Analgesia (19/22)

No further information

References:

Relevant guidelines

Deutsche Gesellschaft zum Studium des Schmerzes, www.dgss.org

Schmerztherapie bei Tumorerkrankungen http://www.krebsgesellschaft.de/download/ll_n_02.pdf
Diarrhea (20/22)

No further information

References:

Relevant Guidelines


**Constipation (21/22)**

*Further information:*

Constipation is not infrequently encountered during chemotherapy. Particularly around the time in autumn and winter, when indoor heating begins and air humidity is consequentially reduced. Sufficient fluid uptake should be encountered by treating health care providers. Opioid therapy usually results in constipation and regular digestion should always be aimed at.

A Cochrane meta-analysis investigated differential efficacy of different agents, the authors concluded, that „The findings of our work indicate that Polyethylene glycol is better than lactulose in outcomes of stool frequency per week, form of stool, relief of abdominal pain and the need for additional products. On subgroup analysis, this is seen in both adults and children, except for relief of abdominal pain. Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.“

More recently, the use of parenteral methylnaltrexone for the management of constipation in palliative care patients was evaluated. Subcutaneous methylnaltrexone; an opioid-receptor antagonist, is now licensed for the treatment of opioid-induced constipation in palliative care when response to usual laxative therapy is insufficient. The authors concluded, that „Here it found that subcutaneous methylnaltrexone is effective in inducing laxation in palliative care patients with opioid-induced constipation and where conventional laxatives have failed. However, the safety of this product is not fully evaluated. Large, rigorous, independent trials are needed.“

*References:*


Candy B, Jones L, Goodman ML, Drake R, Tookman A. Laxatives or methylnaltrexone for the management of constipation in palliative care patients. *Cochrane Database of Systematic Reviews* 2011, Issue 1.
Palliative Care (22/22)

Further information

Growing evidence and increasing awareness in international recommendations underlines the relevance of combined standard oncology care and palliative care. This should be considered early in the course of illness for any patient with metastatic cancer and/or high symptom burden. It is evident that the access to palliative care, including effective control of pain and other symptoms, is important in the treatment of metastatic breast cancer patients.

References:

Smith et al, J Clin Oncol 30 880-887, 2012