Standards of Care and Future Perspectives in Supportive Care

Karin Jordan

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Many aspects of supportive care

- Nutrition
  - Anaemia
- Cardiotoxicity
- Diarrhoe/Obstipation
- Neurotoxicity
- Fertility
- Fatigue
- Antiemesis
- Pulmonary Tox.
- Infections
  - Neutropenia
  - Tumorlysis
  - Thrombocytopenia
- Paravasation
- Supportive measures in radiation therapy
  - Bone complications
- Pain
  - Venous Thromboembolism
- New Toxicities (Targeted drugs)
- Psychological support
- Renal toxicity
- Lymphedema
Supportive care improves patient-reported outcomes in cancer patients!
Definition of Supportive Care, MASCC

“Supportive care in cancer is the prevention and management of the adverse effects of cancer and its treatment. This includes management of physical and psychological symptoms and side effects across the continuum of the cancer experience from diagnosis through treatment to post-treatment care. Supportive care aims to improve the quality of rehabilitation, secondary cancer prevention, survivorship, and end-of-life care”

MASCC = Multinational Association of Supportive Care in Cancer
HISTORIC EXAMPLE OF SUPPORTIVE CARE
Development of Antiemetics

- Actinomycin
- Nitrogen Mustard
- Cisplatin

1950
70ies
80ies
90ies
> 2000

Ø Cannabinoids Metoclopramide + High-dose Metoclopramide Steroids + 5-HT3-Antagonists NK-1-RA

Actinomycin Nitrogen Mustard Cisplatin
PRACTICAL TOOL IN SUPPORTIVE AND PALLIATIVE CARE

- Guidelines -
Palliative and supportive care

Management of Febrile Neutropaenia: ESMO Clinical Practice Guidelines

Published in 2016 – Ann Oncol (2016) 27 (suppl 5): v111-v118
Authors: J. Klagesky, J. de Naurois, K. Rolston, B. Rapoport, G. Maschmeyer, M. Aapro and J. Herrstedt

MASCC and ESMO Consensus Guidelines for the Prevention of Chemotherapy and Radiotherapy-Induced Nausea and Vomiting: ESMO Clinical Practice Guidelines

Published in 2016 – Ann Oncol (2016) 27 (suppl 5): v119-v133
# ESMO Clinical Practice Guidelines: Supportive Care and Palliative Care

<table>
<thead>
<tr>
<th>Title</th>
<th>Author</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Venous Access in Oncology: ESMO Clinical Practice Guidelines</td>
<td>B. Sousa</td>
<td>2015</td>
</tr>
<tr>
<td>ESMO Clinical Practice Guidelines for the Management of Refractory Symptoms at the End of Life and the Use of Palliative Sedation</td>
<td>N.I. Cherny</td>
<td>2014</td>
</tr>
<tr>
<td>ESMO Clinical Practice Guidelines on Palliative Care: Advanced Care Planning</td>
<td>D. Schrijvers</td>
<td>2014</td>
</tr>
<tr>
<td>Bone Health in Cancer Patients: ESMO Clinical Practice Guidelines</td>
<td>R. Coleman</td>
<td>2014</td>
</tr>
</tbody>
</table>
Guidelines on a national level

S3 Leitlinie »Supportive Therapie bei onkologischen PatientInnen«
Our decision: 10 subjects

1. Anemia
2. Antiemesis
3. Neutropenia
4. Dermal toxicities
5. Mucositis
6. Chemotherapy induced diarrhoea
7. Peripheral neurotoxicity
8. Bone complications
9. Supportive measures in radiation oncology
10. Extravasation

S3 Guideline "Supportive Therapy": Karin Jordan Guideline coordinator, Franziska Jahn Guideline secretary 2016, AWMF Register-No: 032-0540L
Willkommen auf der homepage der S3 Leitlinie „Supportive Therapie bei onkologischen Patient:innen“. Im Rahmen des Leitlinienprogrammes Onkologie werden in den nächsten 2-3 Jahren zu 10 wichtigen Themen aus dem Bereich der Supportiven Therapie Handlungs- und Therapieempfehlungen erarbeitet, um eine bessere Versorgung von onkologischen Patient:innen zu erreichen.

Das Projekt im Rahmen des Leitlinienprogrammes Onkologie mit ca. 60 Mitarbeiter:innen und Mandatsträger:innen aller relevanten Fachgesellschaften und Arbeitsgruppen sowie Vertreter:innen von Patient:innenorganisationen ist unter das Mandat der Arbeitsgemeinschaft Supportive Maßnahmen in der
Let’s get practical
Supportive Care - Content

1. Anaemia
2. Fatigue
3. Neurotoxicity
4. Febrile neutropenia
CHEMOTHERAPY-INDUCED ANAEMIA
3 Options

Chemotherapy-induced Anaemia

- ESA
- i.v. Iron + ESA
- Transfusion

ESA: Erythropoiesis stimulating agent
Most Upto Date Anaemia Guidelines

NICE National Institute for Health and Care Excellence

Erythropoiesis-stimulating agents (epoetin and darbeopoeitin) for treating anaemia in people with cancer having chemotherapy (including review of TA142)

Issued: November 2014

Konsultationsfassung S3-Leitlinie Supportive Therapie bei onkologischen PatientInnen

Version 0.1 - Juni-2016
AWMF-Registernummer: 032-054OL

German S3 Guideline Supportive Therapy: Summer 2016

Metaanalysis of 65 ESA studies
State of the Art: ESA
Metaanalysis of 65 ESA studies

Only ESA-studies within current approval were included (Start Hb < 10 g/dl, Target Hb 12 g/dl):

• Hb-Level increase
• Reduced need for red blood cell transfusions
• No disadvantage for overall survival (OR 0.99, 95% CI 0.89–1.10)
• Improvement of therapy-associated fatigue

BUT
• ↑ Risk of thromboembolic events (RR 1.53, 95 % CI 1.02 – 2.31)
• ↑ Hypertension
For daily practice

Chemotherapy-induced Anaemia

ESA

i.v. Iron + ESA

Transfusion

Benefit versus Risk:
- Potential quality of life ↑
- Transfusion ↓
- Potential adverse events ↑

Possible with functional iron deficiency

Transfusion of 1 erythrocyte concentrate

NICE guideance and S3 guideline "Supportive S3 Guideline "Supportive Therapy": Karin Jordan Guideline coordinator, Franziska Jahn Guideline secretary 2016, AWMF Register-No: 032-054OL
When considering the use of ESA it is recommended to inform the patient about the potential risks (thromboembolic complications and hypertension) and potential benefits (potential increase of quality of life and reduction of transfusion rate).

GRADE 

1.2.1. Grade of recommendation

A

Evidenzbasierte Empfehlung

When considering the use of ESA it is recommended to inform the patient about the potential risks (thromboembolic complications and hypertension) and potential benefits (potential increase of quality of life and reduction of transfusion rate).

GRADE

⊕⊕⊕⊕

Literatur: (Tonia, Mettler et al. 2012, Moebus, Jackisch et al. 2013, Nitz, Cluz et al. 2014)

Plenary vote

Strong consensus
1.3.1. Evidenzbasierte Empfehlung

Grade of recommendation

0

For the treatment of chemotherapy induced anemia ESAs can be considered.

GRADE ⊕⊕⊝⊝

Literatur: (Tonin, Mettler et al. 2012, Moebus, Jackisch et al. 2013, Nitz, Gluz et al. 2014)

Plenary vote

Strong consensus

S3 Guideline "Supportive Therapy": Karin Jordan Guideline coordinator, Franziska Jahn
Guideline secretary 2016, AWMF Register-No: 032-054OL
FATIGUE
Therapeutic approaches:

1. Therapy of concomitant factors (depression, anaemia,...)
2. Pharmacological intervention
3. Mind-body intervention
4. Psychosocial intervention
5. Physical activity
NEUROTOXICITY
Prevention of polyneuropathy from platinum derivates

- Acetylcysteine
- Amifostine
- Amitryptiline
- Carbamazepine
- Gluthatione (GSH)
- Vitamin E
- Nimodipine
- **Calcium and magnesium** (Loprinzi, JCO 2013)

No effective prevention available

*Hershman DL., JCO 2014;*
S3 Guideline "Supportive Therapy": Karin Jordan Guideline coordinator, Franziska Jahn
Guideline secretary 2016, AWMF Register-No: 032-054OL
Therapy of painful polyneuropathy (PNP)

Moderate level of recommendation
- Duloxetine (sSRI*) effective
  Dosage: 30 mg week 1, 60 mg week 2§

Worth a try**
- Tricyclic antidepressants (e.g. nortriptyline or desipramine)
- Gabapentin and Pregabalin
- Topical gel: Baclofen (10 mg), Amitriptylin HCL (40 mg) and Ketamin (20 mg)

* sSRI: Selective Serotonin Reuptake Inhibitor
** Explored evidence: no studys for chemotherapy-induced PNP

Neuropathic pain and Menthol

- Topical application of a 1 % menthol cream in 51 Patients with chronic neuropathic pain and CTX

→ Significant improvement in pain score after treatment in 82 % of the patients (p < 0.001)

→ Assumed mode of action: stimulation of the cold-menthol-receptor (TRPM8).

Transient receptor potential melastatin 8 Receptor = Menthol Receptor
Neuropathic pain and Menthol


- Topical application of a 1% menthol cream in 51 patients with chronic neuropathic pain and CTX

  - Significant improvement in pain score after treatment in 82% of the patients (p < 0.001)

  - Assumed mode of action: stimulation of the cold-menthol receptor (TRPM8).

→ Menthol cream is worth a try

Menthol 1 g
DAC based cream 100 g

Transient receptor potential melastatin 8 Receptor = Menthol Receptor
FEBRILE NEUTROPENIA
clinical practice guidelines

Management of febrile neutropaenia: ESMO Clinical Practice Guidelines†

J. Klastersky1, J. de Naurois2, K. Rolston3, B. Rapoport4, G. Maschmeyer5, M. Aapro6 & J. Herrstedt7 on behalf of the ESMO Guidelines Committee*

1Institut Jules Bordet – Centre des Tumeurs de l’ULB, Brussels, Belgium; 2St Luke’s Cancer Centre, Royal Surrey County Hospital, Guildford, UK; 3M.D. Anderson Cancer Center, Houston, TX, USA; 4Medical Oncology Centre of Rosebank, Johannesburg, South Africa; 5Department of Hematology, Oncology and Palliative Care, Ernst von Bergmann Hospital, Potsdam, Germany; 6Multidisciplinary Institute of Oncology, Clinique de Genolier, Genolier, Switzerland; 7Department of Oncology, Odense University Hospital (OJH), Odense, Denmark
Assess frequency of FN associated with the planned chemotherapy regimen

- FN risk $\geq$ 20%
- FN risk 10-20%
- FN risk $\leq$ 10%

Assess factors that increase the frequency/risk of FN
- Age $>$ 65 years
- Other comorbidities

Define the patient's overall FN risk for planned chemotherapy regimen

- Overall FN risk $\geq$ 20%
- Overall FN risk $<$ 20%

Prophylactic G-CSF recommended
G-CSF prophylaxis not indicated

Reassess at each cycle
## Indications for prophylactic administration of GCSF

**S3 guidelines**

<table>
<thead>
<tr>
<th>Risk of febrile neutropenia</th>
<th>Recommendation</th>
<th>Examples</th>
</tr>
</thead>
</table>
| High > 40 %                 | G-CSF          | • MAID  
                           |                | • BEACOPP       |
| Moderate 20-40 %            | G-CSF          | • TAC   
                           |                | • CHOP (qd14)   |
| Intermediate 10-20 %        | G-CSF when individual risk factors are present | • FOLFOX  
                           |                | • FOLFIRI       |
| Low < 10 %                  | NO administration of GCSF | • Carboplatin/Etoposid |
Still controversial: Definition of individual risk factors

<table>
<thead>
<tr>
<th>ASCO-2015</th>
<th>EORTC-2010</th>
<th>NCCN-2016</th>
</tr>
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<tbody>
<tr>
<td>• Age 65 years</td>
<td>• Older age (≥65 years)</td>
<td>• Prior chemotherapy or radiation therapy</td>
</tr>
<tr>
<td>• Advanced disease</td>
<td>• Advanced disease/metastasis</td>
<td>• Persistent neutropenia</td>
</tr>
<tr>
<td>• Previous chemotherapy or radiation therapy</td>
<td>• Prior episode of FN</td>
<td>• Bone marrow involvement by tumor</td>
</tr>
<tr>
<td>• Preexisting neutropenia or bone marrow</td>
<td>• No antibiotic prophylaxis</td>
<td>• Recent surgery and/or open wounds</td>
</tr>
<tr>
<td>involvement with tumor</td>
<td>• No G-CSF use</td>
<td>• Liver dysfunction (bilirubin &gt;2.0)</td>
</tr>
<tr>
<td>• Infection</td>
<td>• Poor performance and/or nutritional status</td>
<td>• Renal dysfunction (creatinine clearance &lt;50)</td>
</tr>
<tr>
<td>• Open wounds or recent surgery</td>
<td>• Female gender</td>
<td>• Age &gt;65 years receiving full chemotherapy</td>
</tr>
<tr>
<td>• Poor performance status or poor nutritional</td>
<td>• Haemoglobin &lt;12 g/dL/anaemia</td>
<td>dose intensity</td>
</tr>
<tr>
<td>status</td>
<td>• Cardiovascular disease</td>
<td>• Other:</td>
</tr>
<tr>
<td>• Poor renal function</td>
<td>• Renal disease</td>
<td>• Poor performance status</td>
</tr>
<tr>
<td>• Liver dysfunction, most notably elevated</td>
<td>• Abnormal liver transaminases</td>
<td>• HIV - infections</td>
</tr>
<tr>
<td>bilirubin</td>
<td>• Low pre-treatment or pre-cycle ANC</td>
<td></td>
</tr>
<tr>
<td>• Cardiovascular disease</td>
<td>• Serum albumin &lt;3.5 g/dL</td>
<td></td>
</tr>
<tr>
<td>• Multiple comorbid conditions</td>
<td>• Prior chemotherapy</td>
<td></td>
</tr>
<tr>
<td>• HIV infection</td>
<td>• Prior infection</td>
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Relevance of individual risk factors

= individual risk factor for febrile neutropenia
### Individual risk factors

#### Consensus-based Statement

<table>
<thead>
<tr>
<th><strong>EK</strong></th>
<th>An individual risk factor can not be clearly identified. The following factors, in particular when they occur in combination, probably increase the risk for febrile neutropenia:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Age &gt; 65 years</td>
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<tr>
<td></td>
<td>• Low performance status (low Karnofsky Index, high ECOG)</td>
</tr>
<tr>
<td></td>
<td>• Comorbidities (COPD, Heart failure NYHA III-IV, HIV disease, Autoimmune disease, significantly impaired renal function)</td>
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<tr>
<td></td>
<td>• Highly advanced symptomatic tumor disease</td>
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<tr>
<td></td>
<td>• Chemotherapy in the past</td>
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<tr>
<td></td>
<td>• Laboratory parameters (anemia, lymphocytopenia &lt; 700/µl, hypalbuminemia, hyperbilirubinaemia)</td>
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S3 Guideline "Supportive Therapy": Karin Jordan Guideline coordinator, Franziska Jahn Guideline secretary 2016, AWMF Register-No: 032-054OL
„Supportive Care makes Excellent Cancer Care possible“ (MASCC)
SAVE THE DATE

2017
22-24 JUNE
WASHINGTON DC, USA
SUPPORTIVE CARE MAKES EXCELLENT CANCER CARE POSSIBLE

MASCC/IS00
ANNUAL MEETING ON SUPPORTIVE CARE IN CANCER

www.mascc.org/meeting