Integrating supportive care in the treatment of lung cancer patients

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Member ESMO supportive care Faculty
Board member and Past-President of MASCC
( Multinational Association for Supportive Care in Cancer )
And Honorary President of AFSOS
(French-speaking Association for Supportive Care)
COI for this talk

◆ Consultant and/or investigator or speaker for:
  Amgen, Hospira, JnJ, Kyowa Hakko Kirin, Mundipharma, Novartis,
  Roche, Sandoz, Taiho, Teva

◆ Executive Committee member of
  MASCC and AFSOS
  and ESMO supportive care Faculty
TOPICS

- The key role of supportive care
- BONE
- ANTIEMETICS
- FN PREVENTION
- PAIN
- DYSPNEA
Supportive care and palliative care: a time for unity in diversity

emotional burden of patients and caregivers, helps cancer survivors with psychological and social problems [1].

Matti S. Aapro
IMO Clinique de Genolier, Department of Medical Oncology
Survie Globale

« Early Palliative Care »

Temel J et al. NEJM 2010

- Standard Care
- Early Palliative Care
TOPICS

- The key role of supportive care
- BONE
  - ANTIEMETICS
  - FN PREVENTION
  - PAIN
  - DYSPNEA
Bone health in cancer patients: ESMO Clinical Practice Guidelines†

R. Coleman1, J. J. Body2, M. Aapro3, P. Hadji4 & J. Herrstedt5 on behalf of the ESMO Guidelines Working Group*

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## Incidence of bone metastasis in cancer

**Table: Metastatic Bone Disease Prevalent in Patients with Lung Cancer**

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Incidence of BM in Cancers (%)</th>
<th>Median Survival (months)</th>
<th>5-year Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myeloma</td>
<td>95-100</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Prostate</td>
<td>65 - 75</td>
<td>40</td>
<td>25</td>
</tr>
<tr>
<td>Breast</td>
<td>65 - 75</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td>Thyroid</td>
<td>60</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
<td><strong>Lung</strong></td>
<td><strong>30 - 40</strong></td>
<td><strong>&lt;6</strong></td>
<td><strong>&lt;5</strong></td>
</tr>
<tr>
<td>Kidney</td>
<td>20 - 25</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Melanoma</td>
<td>14 - 45</td>
<td>&lt;6</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>

Coleman, Cancer 1997
NTX Normalization Within 3 Months Is Associated With Improved Survival


Abbreviations: E-E, Patients whose NTX levels remained elevated at 3 months; E-N, Patients whose NTX levels normalized at 3 months from elevated baseline levels; NSCLC, Non-small cell lung cancer; NTX, N-telopeptide of type I collagen; OST, Other solid tumors.
Lung cancer post-hoc subgroup of randomised, double-blind, active-controlled, Phase 3 trial

- **Key inclusion**
  - Adults with lung cancer and bone metastases
- **Key exclusion**
  - Current or prior intravenous bisphosphonate administration

### Lung cancer type, n (%)

<table>
<thead>
<tr>
<th>Lung cancer type, n (%)</th>
<th>Zoledronic acid</th>
<th>Denosumab</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NSCLC</strong></td>
<td>352 (88)</td>
<td>350 (85)</td>
<td>702 (100)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>211 (60)</td>
<td>189 (54)</td>
<td>400 (57)</td>
</tr>
<tr>
<td>Squamous Cell</td>
<td>75 (21)</td>
<td>88 (25)</td>
<td>163 (23)</td>
</tr>
<tr>
<td>Other</td>
<td>66 (19)</td>
<td>73 (21)</td>
<td>139 (20)</td>
</tr>
<tr>
<td><strong>SCLC</strong></td>
<td>48 (12)</td>
<td>61 (15)</td>
<td>109 (100)</td>
</tr>
</tbody>
</table>

Calcium (500 mg) and Vitamin D (400 IU) strongly recommended

---

Scagliotti, WCLC 2011
Overall survival: patients with NSCLC
Retrospective analysis (Scagliotti et al)

HR, 0.78 (95% CI, 0.65–0.94)

$P = 0.0104$

KM estimate of median, months

- **Denosumab**: 9.5 months
- **Zoledronic acid**: 8.1 months

Patients at risk:
- **Zoledronic acid**: 352, 275, 185, 123, 91, 40, 23, 12
- **Denosumab**: 350, 278, 203, 148, 110, 66, 39, 24
Overall survival: NSCLC by histological types

Adenocarcinoma

- KM estimate of median, months
  - Denosumab: 9.6
  - Zoledronic acid: 8.2

Proportion of patients survived

HR, 0.80 (95% CI, 0.62–1.02)

Study month

Patients at risk:
- Zoledronic acid: 211 169 113 71 55 21 14 8
- Denosumab: 189 154 114 83 59 40 22 16

Squamous cell carcinoma

- KM estimate of median, months
  - Denosumab: 8.6
  - Zoledronic acid: 6.4

Proportion of patients survived

HR, 0.68 (95% CI, 0.47–0.97)

Study month

Patients at risk:
- Zoledronic acid: 75 56 38 28 17 7 4 2
- Denosumab: 88 66 47 34 25 13 10 3

Scagliotti et al, WCLC 2011
SPLENDOUR: Phase III trial of denosumab in patients with Stage IV NSCLC

- Primary objective: overall survival
- Secondary objectives: PFS (RECIST 1.1); safety (CTCAE v 4); determination of biomarkers for translational research

Stage IV untreated NSCLC ± bone metastases (N~1000)

Stratify:
- Bone metastases
- Region
- ECOG PS
- Histology

4–6 CT Q3W + BSC (zoledronic acid allowed)

4–6 cycles CT Q3W + denosumab 120 mg SC Q3 (–4) weeks

†To be continued on tumour progression and concomitantly to subsequent lines of systemic treatment.

CT, chemotherapy; ECOG, Eastern Cooperative Oncology Group; IV, intravenously; Q3W, every 3 weeks; SC, subcutaneously.
TOPICS

- The key role of supportive care
- BONE
- ANTIEMETICS
- FN PREVENTION
- PAIN
- DYSPNEA
CINV Control
PROGRESS SINCE the 80’s

CINV complete control
Over 5 days

Cisplatin (HEC)
Protocol “AC”

1978
CINV complete control
Over 5 days

- 1978: CINV complete control Over 5 days
  - 0%
  - 10%

- 1988:
  - HD-MCP + Dex: 50% 50%
  - Protocol “AC”: 50%

- 1998:
  - Setron + Dex: 60% 50%

- 2008:
  - Setron + Dex + NK1RA: 85% 75%

HD-MCP = Hi dose Metoclopramide haute dose
Dex = Dexamethasone
CINV Chemo induced Nausea and Vomiting

MASCC/ESMO ANTIEMETIC GUIDELINE 2016

Multinational Association of Supportive Care in Cancer

Organizing and Overall Meeting Chairs:
Matti Aapro, MD
Richard J. Gralla, MD
Jørn Herrstedt, MD, DMSci
Alex Molassiotis, RN, PhD
Fausto Roila, MD

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# ACUTE Nausea and Vomiting: SUMMARY

<table>
<thead>
<tr>
<th>EMETIC RISK GROUP</th>
<th>ANTIEMETICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Non-AC</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX + NK&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
<tr>
<td>High AC</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX + NK&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX + NK&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
<tr>
<td>Moderate (other than carboplatin)</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX</td>
</tr>
<tr>
<td>Low</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; or DEX or DOP</td>
</tr>
<tr>
<td>Minimal</td>
<td>No routine prophylaxis</td>
</tr>
</tbody>
</table>

| 5-HT<sub>3</sub> = serotonin<sub>3</sub> receptor antagonist | DEX = Dexamethasone | NK<sub>1</sub> = neurokinin<sub>1</sub> receptor antagonist such as APREPITANT or FOSAPREPITANT or ROLAPITANT or NEPA (combination of netupitant and palonosetron) | DOP = dopamine receptor antagonist |

**NOTE:** If the NK<sub>1</sub> receptor antagonist is not available for AC chemotherapy, palonosetron is the preferred 5-HT<sub>3</sub> receptor antagonist.
# DELAYED Nausea and Vomiting: SUMMARY

<table>
<thead>
<tr>
<th>Emetic Risk Group</th>
<th>Antiemetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Non-AC</td>
<td><strong>DEX</strong> or (if APR 125mg for acute: (<strong>MCP</strong> + <strong>DEX</strong>) or <strong>APR</strong>)</td>
</tr>
<tr>
<td>High AC</td>
<td>None or (if APR 125mg for acute: <strong>DEX</strong> or <strong>APR</strong>)</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>None or (if APR 125mg for acute: <strong>APR</strong>)</td>
</tr>
<tr>
<td>Oxaliplatin, or anthracycline, or cyclophosphamide</td>
<td><strong>DEX</strong> can be considered</td>
</tr>
<tr>
<td>Moderate (other)</td>
<td>No routine prophylaxis</td>
</tr>
<tr>
<td>Low and Minimal</td>
<td>No routine prophylaxis</td>
</tr>
</tbody>
</table>

**DEX** = Dexamethasone  
**MCP** = Metoclopramide  
**APR** = Aprepitant
COMMITTEE IX (1a/3): Advanced Cancer

Treatment of Nausea and Vomiting in Advanced Cancer: Drugs of Choice

The antiemetic drug of choice in advanced cancer is metoclopramide (titrated to effect).

MASCC Level of Consensus: High
MASCC Level of Confidence: Moderate
ESMO Level of Evidence: III
ESMO Grade of Recommendation: C
COMMITTEE IX (1b/3): Advanced Cancer

Treatment of Nausea and Vomiting in Advanced Cancer: Drugs of Choice

Alternative options include haloperidol, levomepromazine, or olanzapine.

MASCC Level of Consensus: High
MASCC Level of Confidence: Low
ESMO Level of Evidence: V
ESMO Grade of Recommendation: D

The use of cyclizine or 5-HT$_3$ receptor antagonists is poorly defined to date and may be used when dopamine antagonists are contraindicated or ineffective.

MASCC Level of Consensus: Low
MASCC Level of Confidence: Low
ESMO Level of Evidence: V
ESMO Grade of Recommendation: D

**NOTE:** The evidence to support combinations of drugs with antiemetic effect and different mechanisms of action is minimal (except in bowel obstruction)
COMMITTEE IX (3/3): Advanced Cancer

Treatment of Nausea and Vomiting in Advanced Cancer: Opioid-induced Emesis

No recommendation can be made about specific antiemetics, although various antiemetics may help. Opioid rotation and route switching may be effective approaches. There is no data to support prophylactic antiemetics in this situation.

MASCC Level of Consensus: High
MASCC Level of Confidence: Low
ESMO Level of Evidence: V
ESMO Grade of Recommendation: D
TOPICS

◆ The key role of supportive care
◆ BONE
◆ ANTIEMETICS

◆ FN PREVENTION
◆ PAIN
◆ DYSPNEA
Indications for Primary Prophylaxis of FN by hGFs*

- Reasonable only if
  - Probability of FN of ~20% based on chemotherapy and/or special situations, or
  - Dose reduction deemed detrimental to outcome [A]

- Efficacy parameters
  - Affected
    - ANC recovery [I]
    - Fever [I]
    - Infection rate [I]
    - Use of intravenous (IV) antibiotics [II]
    - Hospital discharge [I]
  - Controversial
    - Infectious mortality [I]
    - Early mortality
  - Not affected
    - Survival [I]

Special Situations for the Use of hGFs for Standard Therapy

<table>
<thead>
<tr>
<th>Indication</th>
<th>Special Situation</th>
<th>Use of hGF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary prophylaxis</td>
<td>Reduced marrow reserve (eg, ANC &lt; 1.5 × 10^9/L) due to radiotherapy of &gt; 20% marrow</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Human immunodeficiency virus</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Patients aged ≥ 65 years treated with curative intention (CHOP or more-intensive regimens for patients with aggressive NHL)</td>
<td>Yes</td>
</tr>
<tr>
<td>Secondary prophylaxis</td>
<td>Further infections in the next treatment cycle considered life threatening</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Dose reduction below threshold</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Delay in chemotherapy</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Lack of protocol adherence if compromising cure rate, OS, or disease-free survival</td>
<td>Yes</td>
</tr>
<tr>
<td>Therapy of afebrile neutropenia</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>Therapy of FN</td>
<td>General</td>
<td>No</td>
</tr>
<tr>
<td>Therapy of high-risk FN</td>
<td>Protracted FN (&gt; 7 days), hypotension, sepsis, pneumonia, or fungal infection</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Roman numerals are the levels of evidence and the letters are their grades for recommendations. Everything not labelled as such is based on reasonable consensus/clinical practice.

Patient Assessment Algorithm to Decide If Primary Prophylactic G-CSF Usage Is Warranted

**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 increase the frequency/risk of FN

<table>
<thead>
<tr>
<th>High risk</th>
<th>Age &gt; 65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased risk (level I and II evidence)</td>
<td>Advanced disease</td>
</tr>
<tr>
<td>History of prior FN</td>
<td>No antibiotic prophylaxis, no G-CSF use</td>
</tr>
<tr>
<td>Other factors (level III and IV evidence)</td>
<td>Poor performance and/or nutritional status</td>
</tr>
<tr>
<td>Female gender</td>
<td>Haemoglobin &lt; 12 g/dL</td>
</tr>
<tr>
<td>Liver, renal, or cardiovascular disease</td>
<td></td>
</tr>
</tbody>
</table>

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

- **Overall FN risk ≥ 20%**
  - Prophylactic G-CSF recommended
- **Overall FN risk < 20%**
  - G-CSF prophylaxis not indicated

*Secondary prophylaxis: start G-CSF if a neutropenic event was observed in the previous cycle*

TOPICS

- The key role of supportive care
- BONE
- ANTIEMETICS
- FN PREVENTION

PAIN

- DYSPNEA
Management of cancer pain: ESMO Clinical Practice Guidelines†

C. I. Ripamonti¹, D. Santini², E. Maranzano³, M. Berti⁴ & F. Roila⁵, on behalf of the ESMO Guidelines Working Group*
An overview of cancer pain prevalence

<table>
<thead>
<tr>
<th>PHASE</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>After curative treatment</td>
<td>33%</td>
</tr>
<tr>
<td>On anticancer treatment</td>
<td>59%</td>
</tr>
<tr>
<td>Metastatic, advanced or terminal phase</td>
<td>64%</td>
</tr>
</tbody>
</table>

Prevalence of cancer pain: Meta-analysis of 52 studies

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>% Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head/neck</td>
<td>70 %</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>59 %</td>
</tr>
<tr>
<td>Lung/bronchus</td>
<td>55 %</td>
</tr>
<tr>
<td>Breast</td>
<td>54 %</td>
</tr>
<tr>
<td>Urogenital</td>
<td>52 %</td>
</tr>
<tr>
<td>Gynaecological</td>
<td>60 %</td>
</tr>
</tbody>
</table>

Despite clear recommendations from the World Health Organization, cancer pain control is still a major issue.

Treatment of cancer pain

**STRONG RECOMMENDATION**

Mild pain → STEP 1 NRS 1-3 → NSAIDs - PARACETAMOL

- **STEP 2** NRS 4-6 → WEAK OPIOIDS +/- NSAIDs - PARACETAMOL
- **STEP 3** NRS 7-10 → STRONG OPIOIDS +/- NSAIDs - PARACETAMOL

**PERIODICAL REASSESSMENT**

- Use rescue medications. If pain not controlled, go on the next step

**WEAK RECOMMENDATION**

Mild-Moderate pain → **STEP 2** NRS 4-6 → WEAK OPIOIDS +/- NSAIDs - PARACETAMOL

- Periodical reassessment of cancer pain. Use rescue medications. If pain not controlled, do not change opioid but go on the next step

**STRONG RECOMMENDATION**

Moderate-Severe pain → **STEP 3** NRS 7-10 → STRONG OPIOIDS +/- NSAIDs - PARACETAMOL

- Increase the dose of opioid every day, considering the number of opioid rescue doses used, till pain control or side effects

**SIDE EFFECTS**

- Reasses the pain intensity and its causes
- Consider the type and/or doses of adjuvants
- Consider opioid or route of opioid administration switching
- Consider invasive interventions
- Team decision

**PERSISTING PAIN**

- Use always rescue doses to treat Breakthrough Pain

**MILD - MODERATE PAIN**

- Oral or transdermal Long acting opioid
- Symptomatic treatment

**MODERATE - SEVERE PAIN**

- Adjuvant drugs such as corticosteroids, anticonvulsants, antidepressants, should be considered at any step when necessary
TOPICS

- The key role of supportive care
- BONE
- ANTIEMETICS
- FN PREVENTION
- PAIN

DYSPNEA
Dyspnea: the hardest symptom to control?
Causes: CAAPPAAC

Cardiac…
Asthma (+ chronic obstructive pulmonary disease)
Airway obstruction
Pleural effusion
Pulmonary embolism
Anemia
Anxiety
CANCER AND TREATMENT
Evaluating dyspnoea

Medical Research Council (MRC)
American Thoracic Society-Division of Lung Disease (ATS-DLD) questionnaire
Numeric scales (0 to 10)
VAS 0 to 100 mm
Verbal scale: Likert 4 (6) levels: no =1, some=2, a lot=3, extreme=4
Support Team Assessment Schedule (STAS)
EORTC QLQC30
The Borg Category Scale
Chronic Respiratory Questionnaire (CRQ)
The Oxygen Cost Diagram (OCD)
The Baseline Dyspnea Index (BDI)
Symptom relief

Anticholinergic drugs and mucolytics

Physical therapy and methods of respiratory management (Level 1 evidence)

Radiation therapy

Laser desobstruction

Thoracocentesis / pleurodesis (permanent pleural catheters)

Guidelines for treatment/prevention of subsequent pulmonary emboli
Management of venous thromboembolism (VTE) in cancer patients: ESMO Clinical Practice Guidelines

M. Mandalà¹, A. Falanga² & F. Roila³
On behalf of the ESMO Guidelines Working Group*  
¹Unit of Medical Oncology, ²Division Immunohaematology and Transfusion Medicine, Haemostasis and Thrombosis Center, Department of Oncology and Haematology, Ospedali Riuniti, Bergamo; ³Department of Medical Oncology, S. Maria Hospital, Terni, Italy

Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update

Gary H. Lyman, Alok A. Khorana, Nicole M. Kuderer, Agnes Y. Lee, Juan Ignacio Arcelus, Edward P. Bakban, Jeffrey M. Clarke, Christopher R. Flowers, Charles W. Francis, Leigh E. Gates, Ajay K. Rakkar, Nigel S. Key, Mark N. Levine, Howard A. Liebman, Margaret A. Tempa, Sandra L. Wong, Ann Alexis Prestrud, and Anna Falanga
Oxygen therapy for patients who are not hypoxaemic is no more effective than medical air. If a therapeutic trial is indicated, any symptomatic benefit is likely within the first 72 hours.
SYMPTOM RELIEF

Regular, low dose, sustained release oral morphine (Level 1 evidence) titrated to effect (with regular aperients) is effective and safe.
Cancer Care Ontario’s
Symptom Management Guide-to-Practice:
Dyspnea
“Supportive care makes excellent cancer care possible”

Dorothy M.K. Keefe, MASCC president
MASCC/ISOO 2016
International Symposium on Supportive Care in Cancer
Save The Date...Adelaide, Australia - June 23-25 2016
Punctuality