Are the ESMO guidelines adapted to the elderly?

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Clinical practice guidelines

- **Definition**
  - Systemically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances

- **Aim**
  - To assist practitioners in appropriate clinical decision making
  - To improve quality of healthcare and outcomes for patients
  - To influence national policies for efficient allocation of resources and for better delivery systems
Clinical practice guidelines

PROVIDE THE RIGHT CARE,
AT THE RIGHT TIME,
FOR THE RIGHT PERSON
IN THE RIGHT WAY

Eisenberg et al; JAMA 2000
ESMO clinical guidelines
ESMO clinical guidelines

• **Motivation**
  > Important tool for the future development of Medical Oncology
  > Achieve high common standards of medical oncology practices for patients in all European countries

• **History**
  > 1998: H. Hansen created ESMO Clinical Guidelines in the Central & Eastern European Task Force
  > 1999: ESMO Guidelines Task Force
    • ESMO minimum clinical recommendations
  > 2006: ESMO Guidelines Working Group
    • ESMO clinical guidelines
ESMO clinical guidelines

- **Principles**
  - Set of statements for basic standard of care that, according to ESMO, is necessary in all European countries
  - Disease- or topic-oriented
  - Evidence-based
  - Emphasis on medical oncology
  - Regularly updated (once yearly)
ESMO clinical guidelines

• Format
  > Size
    • 3 pages with up to 10 references
  > Content
    • Incidence
    • Diagnosis
    • Staging and risk assessment
    • Treatment
    • Response evaluation
    • Follow-up
  > Level of evidence and grade of recommendation (according to ASCO)
ESMO clinical guidelines

• Process

- Editorial board
  - Subject editors
    - Authors
      - Reviewers
ESMO clinical guidelines

• Process
  > Editorial board
    • Overviews the entire process
    • Final responsibility for content and publication
  > Subject editors
    • Primary contact with authors
    • First revision of manuscripts according to defined rules
    • Second revision of manuscripts taking in consideration the comments of reviewers
    • Discussion of final drafts and open questions with “editorial board” and/or the members of the ESMO Guidelines Task Force

ESMO clinical recommendations
ESMO clinical guidelines

• Process
  > Reviewers
  • 5 ESMO faculty members per topic
  • Review of new or updated drafts within their range of expertise
  • Multidisciplinary, if appropriate
ESMO clinical recommendations

- 1\textsuperscript{st}-6\textsuperscript{th} set (2001 - 2006) 39
- 7\textsuperscript{th} set (2007) 9
- 8\textsuperscript{th} set (2008) 7
- Total 55
ESMO clinical recommendations

- **Publication**
  - Annals of Oncology
  - ESMO folder (2002)
  - Palm OS version (2002-)

- **Translation into national languages**

- **Presentation at meetings and workshops**

- **Interactive guidelines sessions at ESMO congresses**
## ESMO clinical recommendations

<table>
<thead>
<tr>
<th>Condition</th>
<th>Downloads 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary breast cancer</td>
<td>4.707</td>
</tr>
<tr>
<td>Primary colon cancer</td>
<td>3.395</td>
</tr>
<tr>
<td>Metastatic breast cancer</td>
<td>3.089</td>
</tr>
<tr>
<td>Advanced colon cancer</td>
<td>2.729</td>
</tr>
<tr>
<td>Gastric cancer</td>
<td>2.398</td>
</tr>
<tr>
<td>Hematopoietic GFs</td>
<td>2.370</td>
</tr>
<tr>
<td>NSCLC</td>
<td>2.339</td>
</tr>
<tr>
<td>Rectal cancer</td>
<td>2.319</td>
</tr>
<tr>
<td>Epithelial ovarian cancer</td>
<td>2.315</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>2.187</td>
</tr>
<tr>
<td>SCLC</td>
<td>2.083</td>
</tr>
<tr>
<td>Prophylaxis of Chemotherapy -induced nausea/vomiting</td>
<td>2.065</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>2.017</td>
</tr>
<tr>
<td>Cancer pain</td>
<td>1.936</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>1.931</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1.787</td>
</tr>
<tr>
<td>Esophageal cancer</td>
<td>1.778</td>
</tr>
</tbody>
</table>
## ESMO clinical recommendations

<table>
<thead>
<tr>
<th>Condition</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hodgkin’s disease</td>
<td>1.761</td>
</tr>
<tr>
<td>Follicular NHL (newly diagnosed)</td>
<td>1.757</td>
</tr>
<tr>
<td>CLL</td>
<td>1.673</td>
</tr>
<tr>
<td>CML</td>
<td>1.618</td>
</tr>
<tr>
<td>Testicular NSGCT</td>
<td>1.559</td>
</tr>
<tr>
<td>Testicular Seminoma</td>
<td>1.545</td>
</tr>
<tr>
<td>CUP</td>
<td>1.542</td>
</tr>
<tr>
<td>Large-cell NHL (newly diagnosed)</td>
<td>1.518</td>
</tr>
<tr>
<td>AML</td>
<td>1.512</td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>1.464</td>
</tr>
<tr>
<td>Malignant glioma</td>
<td>1.450</td>
</tr>
<tr>
<td>Head-neck cancer</td>
<td>1.405</td>
</tr>
<tr>
<td>Soft-tissue sarcomas</td>
<td>1.372</td>
</tr>
<tr>
<td>Pleural mesothelioma</td>
<td>1.357</td>
</tr>
<tr>
<td>Large-cell NHL (relapsed)</td>
<td>1.355</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>1.251</td>
</tr>
<tr>
<td>Ewing’s sarcoma</td>
<td>1.247</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>66.831</strong></td>
</tr>
</tbody>
</table>
Clinical guidelines for the elderly
ESMO clinical recommendations

- **References to age**
  - Biological age
    - *Breast cancer: postmenopausal women*
  - Chronological age
    - *Large B-cell non-Hodgkin lymphoma: elderly*
Other cancer treatment recommendations

- NCI-PDQ: no specific guidelines for elderly
- Cochrane library
  > Surgery versus primary endocrine therapy for operable primary breast cancer in elderly women (70 years plus) [2007]
- CA - A Cancer Journal for Clinicians
  > Diagnosis and Treatment of Breast Cancer in the Elderly [2003]
### Specific guidelines for elderly?

- **Characteristics of cancer in relation to age**

<table>
<thead>
<tr>
<th></th>
<th>Adults</th>
<th>Elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>Single serious condition</td>
<td>Co-existent with other diseases and conditions</td>
</tr>
<tr>
<td>Clinical impact</td>
<td>Dominant</td>
<td>Influenced by co-morbidities</td>
</tr>
<tr>
<td>Outcome</td>
<td>Potentially lethal</td>
<td>Death due to other causes</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goal</td>
<td>Survival/QoL</td>
<td>QoL/survival</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Severe</td>
<td>Influenced by age-related changes</td>
</tr>
</tbody>
</table>
Treatment outcome in elderly

- Radiotherapy in elderly

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Treatment outcome</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and neck</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>Prostate</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Uterine</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Anal</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Rectal</td>
<td>↓</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>Adjuvant high risk</td>
<td>=</td>
</tr>
</tbody>
</table>

Horiot, J Clin Oncol 2007
## Treatment outcome in elderly

### Surgery in elderly

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Treatment outcome</th>
<th>Toxicity/mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laparoscopic</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Open</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>=</td>
<td>▲ mortality &lt; 3 months</td>
</tr>
</tbody>
</table>

Audiisio, J Clin Oncol 2007
### Treatment outcome in elderly

- **Chemotherapy in elderly**

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Treatment outcome</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Adjuvant</td>
<td>=</td>
<td>↑</td>
</tr>
<tr>
<td>Colon Adjuvant</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>NSCLC Platinum-based</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>NSCLC PS&lt;2</td>
<td>Single agent</td>
<td></td>
</tr>
<tr>
<td>NSCLC Adjuvant</td>
<td>=</td>
<td>=</td>
</tr>
</tbody>
</table>

Lichtman, Com Oncology 2006
Age-related factors influencing pharmacokinetics

- **Absorption**
  - Controllable
    - Concomitant medication (e.g. H2 blockers, proton pump inhibitors)
    - Compliance
  - Not controllable
    - Reduced gastric secretion, gastric emptying, gastrointestinal motility
    - Diminished splanchnic blood flow
    - Decreased absorption surface

- **Distribution**
  - Changes in body composition
    - Doubling fat content
    - Decreased intracellular water
    - Reduction in albumin concentrations
  - Anemia
  - Increase in volume of distribution
    - Lower peak concentration and prolonged terminal t1/2
Age-related factors influencing pharmacokinetics

- **Metabolism**
  - Liver flow reduced
  - Liver size decreases
    - Possible related changes in P450 microsomal systems
  - Polypharmacy
    - P450 inhibitors: grapefruit juice, amiodarone, fluconazole
    - P450 inducers: phenobarbital
    - Drug interactions leading to adverse events

- **Excretion**
  - Decline in glomerular filtration rate
  - Additional effect of co-morbid conditions on renal function
Problems with specific guidelines for the elderly
Problems with specific guidelines for the elderly


Confounding Bias Associated with the Intervention and the Outcome

COMORBID CONDITIONS

LESS TREATMENT SELECTED
(?Suboptimal)

POOR OUTCOMES

Stratification for comorbidity can control bias.
**Influence of co-morbidity on 3-year survival of women with breast cancer**

<table>
<thead>
<tr>
<th>Level of Co-morbidity</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>483</td>
<td>288</td>
<td>124</td>
<td>41</td>
</tr>
<tr>
<td>Median age, years</td>
<td>60</td>
<td>65</td>
<td>69</td>
<td>70</td>
</tr>
<tr>
<td>Risk of breast cancer vs. other causes of death</td>
<td>4.1</td>
<td>1.7</td>
<td>0.8</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Co-morbid conditions include heart disease, diabetes mellitus, other malignancy, and gallbladder disease

Muss et al; JCO 2007
Integrated approach for guidelines development

**Cancer**
- Histology
- Stage
- Prognostic factors
- Predictive factors

**Patient**
- Age
- Co-morbidity
- Frailty
- ADL, IADL
- MMSE, depression scale
- Social structure

**Treatment**

**Outcome**
- Survival
- QoL
- Socio-economic factors

**Guidelines**
- General
- Specific
ESMO cancer treatment guidelines for the elderly?

- Discrepancies between biological and chronological age
- Approaches to increase the knowledge base
  - Analyses of existing data bases
  - Epidemiology and longitudinal studies
  - Prospective clinical trials
  - Pharmacokinetics and drug sensitivity in relation to age and co-morbidity
  - Quality-of-life issues

Most ESMO guidelines are applicable to (elderly) patients without co-morbidity
Age and/or co-morbid/frailty specific ESMO guidelines might be developed based on evidence-based information