Problems related to the management of malignant hemopathies in older patients

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Gent, 25 January 2013

BHS satellite symposium on Elderly
Malignant Hemopathies in older patients

- 33% of cancers occur in people above 75 years
- Hematologic malignancies account for 8% of all cancers and account for 7% of cancer mortality in Europe
- Remain curable diseases in selected cases
- Average age at diagnosis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDS</td>
<td>75 Y</td>
</tr>
<tr>
<td>AML</td>
<td>70 Y</td>
</tr>
<tr>
<td>MM</td>
<td>70 Y</td>
</tr>
<tr>
<td>LNH</td>
<td>67 Y</td>
</tr>
<tr>
<td>CLL</td>
<td>72 Y</td>
</tr>
</tbody>
</table>

1: data INVS 2003, [WWW.ecancer.eu](http://WWW.ecancer.eu)
2: Rodriguez et al, Ann Oncol 2007, 18 (Supp 1) i3-i83: Stauder, oral communication, [WWW.ecancer.eu](http://WWW.ecancer.eu)
Specific problems in the management of older patients

- Aspects related to the person
  - Heterogeneous population in life expectancy and health status (robust-> fragile)

- Aspects related to the disease
  - More advanced stage at diagnosis
  - Unfavorable biological profile

- Aspects related to the treatment
  - Few EBM recommendatons
  - Standard treatments are associated with more side-effects, toxic death or loss of autonomy
  - Dose-reduced treatments are less effective
Balducci Model

Diagnosis of cancer

- **GO-GO** = Fit
  - Full dose Treatment

- **Slow Go** = Vulnerable
  - Support weaknesses reversible and adaptation of dose

- **No Go** = Fragile
  - Support Care

Clinical case: 89 y.o. lady

- **Complaints:**
  - Pain in the neck for 15 days, weight loss, fatigue, dysphagia

- **Medical History**
  - Stage C B CLL (1992) with Grade II WHO anemia treated by EPO
  - Atrial fibrillation treated by Sintron®
  - HTA grade II, treated by IEC

- **Physical examination**
  - 48 Kg (-3), ECOG 1, BP 140/90 mm hg, AF, edema of the lower limbs, large right tonsil
Clinical case: 89 y.o. Lady (continued)

Diagnosis:
- B NHL (n GC) of the right tonsil
- stage II E B (Ann-Arbor), IPI 1/5
- Anemia grade I (WHO) secondary to B CLL

Comprehensive Geriatric Assessment

- G8: 6/17
  score ISAR: 3/6
- PS: 1
- ADL: 6
- IADL: 6
  MMSE à 24/30
  EVA: 6/10
- MNA 5/14
Conclusions:

- A patient of 89 years, partially dependent, suffers from a diffuse B NHL.
- Recent signs of malnutrition and pain, although surrounded but has a fragile situation.
- Malnutrition and loss of autonomy are clearly linked to lymphoma.

• -> Slow Go pts
« Vulnerable » Needs Clear Definition

– A State of decreased physiological reserves arising from cumulative deficits in several systems and resulting in a diminished resistance to stressors *.


– Risk factors

– AGE ≥ 85+ y
– ≥ 1 geriatric Syndrome
– Co-morbidities > 3
– Deficit ≥ 1 ADL
<table>
<thead>
<tr>
<th>GO-GO</th>
<th>Slow-Go</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CLL (German Study Group)</strong></td>
<td></td>
</tr>
<tr>
<td>Hallek et al, Blood 2008, CIRGS &lt;6 (Low score)</td>
<td></td>
</tr>
<tr>
<td><strong>NHL (EORTC)</strong></td>
<td></td>
</tr>
<tr>
<td>Soubeyran et al, J geria oncol 2011;2;1,36</td>
<td>&gt;70 Y CIRGS high score ECOG ¾ Cl anthracycline/clearance &lt;50, thrombopenia or anemia</td>
</tr>
<tr>
<td><strong>Myeloma (European Myeloma Network)</strong></td>
<td>weakness Low physical activity slow walking speed</td>
</tr>
<tr>
<td>Palumbo et al, Blood, 2011, 118,17,4519</td>
<td></td>
</tr>
</tbody>
</table>
Outcome of older NHL?

- 1997
  - 453 pts > 69 y with aggressive B LNH

<table>
<thead>
<tr>
<th></th>
<th>CHOP</th>
<th>CVP</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>47%</td>
<td>32%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>5 Y OS</td>
<td>26%</td>
<td>19%</td>
<td>&lt;.05</td>
</tr>
</tbody>
</table>

*Bastion et al, JCO, 1997

→ NHL, a curable disease in the older pts
Overall survival in patients (60+y) treated with CHOP and R-CHOP.
2010: Hope for Very older people with large B Cell Lymphoma

• **R mini CHOP** for patients with B Diffuse B Lymphoma
  – 150 pts > 80 ans (80-95 y)
  – OS 2 y: 59%
  – 58 deaths: 12 deaths related to febrile neutropenia
  – albumine < 35g/l = main pronostic factor.
  – Geriatric assessment no done!

→ **Rmini CHOP offers a good compromise between efficacy and safety in pts aged over 80 y.**

Peyrade et al, Lancet Oncol, 2011
2011: importance of Prephase!

• **Early death results from**
  - Disease progression before or after chemotherapy
  - Toxicity due to chemotherapy.

• **Risk factors**
  - Stage IV
  - Bulky disease
  - Extranodal involvement
  - PS 2-4
  - IPI 3-5
  - Symptoms B

*Bairey et al, Ann hematol, 2012,*
Therapy related deaths in the NHL-B2 trial26 before and after the introduction of prephase treatment.

Pfreundschuh M Blood 2010;116:5103-5110
Causes of death in our centre?

- **Nb of deaths:**
  19% (15) out of 52 evaluable pts died.
  27% (4) of deaths after 1 mo, 40% (6) at 6 mos and 33% at 12 Mos.

- **Causes of deaths:**
  Progressive disease is the major cause of death (96%).
  Febrile Neutropenia was the cause of death for only one patient.

- **Does G8 score predict mortality?**

<table>
<thead>
<tr>
<th>n= 52</th>
<th>Death N= 15</th>
<th>Alive n= 37</th>
<th>P=0.267</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>G8≥15 N=8</td>
<td>12.5%</td>
<td>87.5%</td>
<td>7</td>
</tr>
<tr>
<td>G8&lt;15 N=44</td>
<td>31.8%</td>
<td>68.2%</td>
<td>30</td>
</tr>
</tbody>
</table>

→ A poor G8 score does not translate into a worse survival!

Maerevoet et al, *SIOG 2011*; Dubruille et al *EHA 2012/SIOG2012*
Causes of death in our centre?

- Association between death and intensity of treatment? (full dose or adapted dose)

<table>
<thead>
<tr>
<th>N= 50 (Go and slow go)</th>
<th>Dead N= 15</th>
<th>Alive N= 34</th>
<th>P = 0.003</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Full dose N= 32</td>
<td>15.6%</td>
<td>84.4%</td>
<td>27</td>
</tr>
<tr>
<td>Reduced: N=18</td>
<td>55.5%</td>
<td>44.4%</td>
<td>8</td>
</tr>
</tbody>
</table>

→ There is a strong correlation between the choice of treatment and mortality: Better survival is observed with full doses even in slow go patients!

Maerevoet, Dubruille, Libert and Bron; SIOG 2011/EHA 2012/SIOG2012
## NHL: a curable disease in the very older

<table>
<thead>
<tr>
<th>Study</th>
<th>Nb of pts</th>
<th>M age</th>
<th>Geriatric assermente tools</th>
<th>Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peyrade 2011</td>
<td>150</td>
<td>83 (80-95)</td>
<td>IADL/PS</td>
<td>Albumine &lt; 35g/l OS: 2 Y:59%</td>
</tr>
<tr>
<td>Nabhan 2011</td>
<td>170</td>
<td>84 (80-95)</td>
<td>IADL/CIRSG/geriatric synd/PS</td>
<td>Loss IADL, Lack of response OS: 3Y:60%</td>
</tr>
<tr>
<td>Winkelmann 2011</td>
<td>143</td>
<td>63 (18-88)</td>
<td>IADL, ADL/CIRGS/PS</td>
<td>Loss IADL, comorbidity</td>
</tr>
</tbody>
</table>
Toxicities and outcomes among > 70 olders with DLBC NHL treated with RCHOP

37 pts over the age 70 y ( average age 79 ) treated with R CHOP compared their experience with 65 patients aged less than 70 years.

<table>
<thead>
<tr>
<th></th>
<th>&gt;70 Y</th>
<th>&lt; 70 Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIRGS</td>
<td>7,5</td>
<td>5,8</td>
</tr>
<tr>
<td>Chronic disease uncon</td>
<td>43%</td>
<td>23%</td>
</tr>
<tr>
<td>Attenued regimen</td>
<td>22%</td>
<td>5%</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>22%</td>
<td>17%</td>
</tr>
<tr>
<td>Grade 2 emese</td>
<td>0%</td>
<td>12%</td>
</tr>
<tr>
<td>Grade 2 neuropathy</td>
<td>22%</td>
<td>8%</td>
</tr>
<tr>
<td>Hospitalisation</td>
<td>54%</td>
<td>32%</td>
</tr>
<tr>
<td>OS 3 Y</td>
<td>73%</td>
<td>89%</td>
</tr>
</tbody>
</table>

Huntington et al, Leukemia and lymphoma 2012
Chemotherapy regimens: treatment decision flow

**Step 1: Choice of regimen**

Comorbidities

- No
  - RCHOP/CHOP
    - Mild Cardiopathy: CEOP or R-CEOP
    - Severe Cardiopathy: CVP or R-CVP
- Yes
  - Diabetes: CHO or R-CHO
  - Neuropathy: CHP or R-CHP

**Step 2: Dosage of chemotherapy**

- ADL
  - 6
  - 5
  - <5

- IADL
  - 7-8
  - 5-6
  - <5

100% 75% 50%

Spina M et al. The Oncologist 2012;17:838-846
**Table 4. Comparison of outcome between patients aged >80 years and patients aged 70–80 years**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>&gt;80 yrs</th>
<th>70–80 yrs</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response rate</td>
<td>83%</td>
<td>80%</td>
<td>.96</td>
</tr>
<tr>
<td>Relapse rate</td>
<td>39%</td>
<td>30%</td>
<td>.49</td>
</tr>
<tr>
<td>5-yr overall survival rate</td>
<td><strong>54%</strong></td>
<td><strong>61%</strong></td>
<td>.24</td>
</tr>
<tr>
<td>5-yr disease-free survival rate</td>
<td>67%</td>
<td>84%</td>
<td>.11</td>
</tr>
<tr>
<td>5-yr event-free survival rate</td>
<td>46%</td>
<td>67%</td>
<td>.06</td>
</tr>
<tr>
<td>5-yr cause-specific survival rate</td>
<td>68%</td>
<td>75%</td>
<td>.91</td>
</tr>
</tbody>
</table>

*Spina M et al. The Oncologist 2012;17:838-846*
Old lady outcome?? (continued)

- **Chemotherapy**
  - Prephase prednisolone 1 mg / kg for 7 days with monitoring for 48 hours
  - Immunochemotherapy : R mCHOP x 6 cycles
  - Supportive care: EPO, GCS F, preventing infection, pneumococcal vaccination

- **Geriatric intervention**
  - Nutritional Support
  - Stop Sintron® and start HBPM

→20 months later, she is living at home, still in remission, hoping to live up to 100 yrs
Conclusions

• Although the majority of hematologic malignancies occur in the older, in selected cases, they remain curable diseases.

• Geriatric assessment can detect hidden problems, sometimes reversible, and thus avoid to push the patient into life-threatening side effects and/or loss of autonomy.

• To identify reversible problems related to the disease is a major issue and can avoid under-treatment of older patients.

• Tolerability is enhanced by supportive care (nutrition, growth factors, infectious prophylaxis, falls prevention, treatment of depression.....)