Paul Calabresi Award

From suboptimal to optimal treatment in older patients with cancer

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Health status-adapted cancer care

Balance of risks and benefits

• Benefits identical whatever age
  – Response to treatment
  – Quality of life improvement

• Risks higher in the elderly

• Heterogeneity of problems encountered
  – Age-related physiological problems
  – Elderly-specific problems at baseline
    • cognition, nutrition, functional impairment, social problems, ...
  – Elderly-specific events during treatment
    • confusion, loss of weight, functional decline, ...
Selection criteria in aggressive lymphomas

To CHOP or not to CHOP

• >70 at least one factor among
  – Poor performance status (WHO 3-4)
  – Cardiac contra-indication to doxorubicin
  – Low creatinine clearance (<50 ml/mn)
  – Neutropenia or thrombopenia
  – Severe comorbidities

• A regional prospective study

How many unfit patients?

189 patients

- Work-up not completed: 14 patients (7.5%)
- Unfit patients: 67 patients (35.5%)
- Fit patients but excluded from phase II trial: 25 patients (13%)

Diffuse large B-cell and peripheral T-cell non-Hodgkin’s lymphoma in the frail elderly.

*Results of the EORTC 20992 trial with a progressive and cautious strategy.*


EORTC Lymphoma Group
Did we target the right group?

• YES, we did!
  41% PS 3-4
  59.4% ADL dependent
  81% IADL dependent
  93.8% GDS15 ≥ 6
  37.5% MMS < 24

P Soubeyran J Ger Oncol, 2011; 2: 36-44
A cohort study to understand

- Identification in patients with 1\textsuperscript{st} line chemotherapy of predictive factors for
  - Early death
  - Hospitalization for toxicity
  - Functional decline
## Which events to predict?

<table>
<thead>
<tr>
<th>Events</th>
<th>Early death &lt; 6 m.</th>
<th>Functional decline</th>
<th>Hospitalization for toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odd ratio (95% CI)</td>
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</tr>
<tr>
<td>364 patients</td>
<td>59/339</td>
<td>50/299</td>
<td>47/354</td>
</tr>
<tr>
<td>Extension (M+ vs M-)</td>
<td>4.1 (1.65-10.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>2.62 (1.31-5.28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet count &lt; 150 G/l</td>
<td></td>
<td>3.8 (1.3-10.8)</td>
<td></td>
</tr>
<tr>
<td>Clinician opinion</td>
<td>ns</td>
<td></td>
<td>0.51 (0.26-0.99)</td>
</tr>
<tr>
<td>PS</td>
<td>ns</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>MNA ≤ 23.5</td>
<td>2.91 (1.31-56.48)</td>
<td>ns</td>
<td>4.19 (1.7-10.3)</td>
</tr>
<tr>
<td>Get up and go &gt; 20 s</td>
<td>2.51 (1.31-4.82)</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>IADL ≤ 7</td>
<td>ns</td>
<td>3 (1.13-8.09)</td>
<td></td>
</tr>
<tr>
<td>GDS15 ≥ 6</td>
<td>ns</td>
<td>2.4 (1,23-4.66)</td>
<td></td>
</tr>
<tr>
<td>MMS</td>
<td>ns</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>ADL</td>
<td>ns</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIRS-G</td>
<td></td>
<td></td>
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</tbody>
</table>

*Sources: Soubeyran JCO 2012, Soubeyran ASCO2012, Warkus SIOG2011*
### Prediction of toxicity

#### Table 5. Predictive Model

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Prevalence</th>
<th>Grades 3 to 5 Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 72 years</td>
<td>270</td>
<td>54 163 60</td>
</tr>
<tr>
<td>Cancer type GI or GU</td>
<td>185</td>
<td>37 120 65</td>
</tr>
<tr>
<td>Chemotherapy dosing, standard dose</td>
<td>380</td>
<td>76 204 64</td>
</tr>
<tr>
<td>No. of chemotherapy drugs, polychemotherapy</td>
<td>381</td>
<td>70 192 65</td>
</tr>
<tr>
<td>Hemoglobin &lt; 11 g/dL (male), &lt; 10 g/dL (female)</td>
<td>62</td>
<td>12 46 74</td>
</tr>
<tr>
<td>Creatinine clearance (Jelliffe, ideal weight)</td>
<td>44</td>
<td>9 34 77 2.46</td>
</tr>
<tr>
<td>Hearing, fair or worse</td>
<td>123</td>
<td>25 76 62</td>
</tr>
<tr>
<td>No. of falls in last 6 months, 1 or more</td>
<td>91</td>
<td>18 61 67</td>
</tr>
<tr>
<td>IADL: Taking medications, with some help/unable</td>
<td>39</td>
<td>8 28 72</td>
</tr>
<tr>
<td>MOS: Walking 1 block, somewhat limited/limited a lot</td>
<td>109</td>
<td>22 69 63</td>
</tr>
<tr>
<td>MOS: Decreased social activity because of physical/emotional health, limited at least sometimes</td>
<td>218</td>
<td>44 126 58</td>
</tr>
</tbody>
</table>

Mathieu Extermann, *Cancer* 2012;118:3377-86

Prediction of toxicity

Geriatric assessment tools can be useful to manage elderly patients

Table 5. Predictive Model

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Grades 3 to 5</th>
<th>Prevalence</th>
<th>OR</th>
<th>95% CI</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 72 years</td>
<td>270</td>
<td>54 163 60</td>
<td>1.85</td>
<td>1.22 to 2.82</td>
<td>2</td>
</tr>
<tr>
<td>Cancer type GI or GU</td>
<td>185</td>
<td>37 120 65</td>
<td>2.13</td>
<td>1.39 to 3.24</td>
<td>2</td>
</tr>
<tr>
<td>Chemotherapy dosing, standard dose</td>
<td>380</td>
<td>76 204 54</td>
<td>2.13</td>
<td>1.29 to 3.52</td>
<td>2</td>
</tr>
<tr>
<td>No. of chemotherapy drugs, polychemotherapy</td>
<td>351</td>
<td>70 102 55</td>
<td>1.90</td>
<td>1.08 to 2.65</td>
<td>2</td>
</tr>
<tr>
<td>Hemoglobin &lt; 11 g/dL (male), &lt; 10 g/dL (female)</td>
<td>62</td>
<td>12 46 74</td>
<td>2.31</td>
<td>1.15 to 4.64</td>
<td>3</td>
</tr>
<tr>
<td>Creatinine clearance (Jelliffe, ideal weight) &lt; 34 mL/min</td>
<td>44</td>
<td>9 34 77 2.46</td>
<td>1.11 to 5.44</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Hearing, fair or worse</td>
<td>123</td>
<td>25 76 62</td>
<td>1.57</td>
<td>1.04 to 2.60</td>
<td>2</td>
</tr>
<tr>
<td>No. of falls in last 6 months, 1 or more</td>
<td>91</td>
<td>18 61 67</td>
<td>2.47</td>
<td>1.43 to 4.27</td>
<td>3</td>
</tr>
<tr>
<td>IADL: Taking medications, with some help/unable</td>
<td>39</td>
<td>8 28 72</td>
<td>1.50</td>
<td>0.66 to 3.38</td>
<td>1</td>
</tr>
<tr>
<td>MOS: Walking 1 block, somewhat limited/limited a lot</td>
<td>109</td>
<td>22 60 63</td>
<td>1.71</td>
<td>1.02 to 2.96</td>
<td>2</td>
</tr>
<tr>
<td>MOS: Decreased social activity because of physical/emotional health, limited at least sometimes</td>
<td>218</td>
<td>44 126 58</td>
<td>1.36</td>
<td>0.90 to 2.06</td>
<td>1</td>
</tr>
</tbody>
</table>

Abbreviations: GU, genitourinary; IADL, instrumental activities of daily living; MOS, Medical Outcomes Study; OR, odds ratio.

Arti Hurria, J Clin Oncol 2011;29:3457-65
CGA is time-consuming

Screening tools
G8 questionnaire

Eight questions
Performed by a nurse
5 to 10 min
Appetite, weight loss, BMI
Mobility
Mood and cognition
Number of medications
Self-related health
Age

Abnormal if ≤14

Preliminary analysis
Se: 89.6% ; Sp: 60.4%

<table>
<thead>
<tr>
<th>Items</th>
<th>Possible answers (score)</th>
</tr>
</thead>
</table>
| A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties? | 0 : severe decrease in food intake  
1 : moderate decrease in food intake  
2 : no decrease in food intake |
| B Weight loss during the last 3 months                             | 0 : weight loss > 3 kg  
1 : does not know  
2 : weight loss between 1 and 3 kg  
3 : no weight loss |
| C Mobility                                                          | 0 : bed or chair bound  
1 : able to get out of bed/chair but does not go out  
2 : goes out |
| E Neuropsychological problems                                       | 0 : severe dementia or depression  
1 : mild dementia or depression  
2 : no psychological problems |
| F Body Mass Index (BMI (weight in kg) / (height in m²))             | 0 : BMI < 19  
1 : BMI = 19 to BMI < 21  
2 : BMI = 21 to BMI < 23  
3 : BMI = 23 and ≥ 23 |
| H Takes more than 3 medications per day                            | 0 : yes  
1 : no |
| P In comparison with other people of the same age, how does the patient consider his/her health status? | 0 : not as good  
0.5 : does not know  
1 : as good  
2 : better |
| Age                                                                 | 0 : >85  
1 : 80-85  
2 : <80 |
| TOTAL SCORE                                                        | 0 – 17 |

Carine Bellera, Ann Oncol 2012;23:2066-72
The ONCODAGE study

**Gold standard:** Impaired Multidimensional Geriatric Assessment (MGA)

### Items | Possible answers (score)
---|---
A | Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?  
0: severe decrease in food intake  
1: moderate decrease in food intake  
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B | Weight loss during the last 3 months  
0: weight loss > 3 kg  
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C | Mobility  
0: bed or chair bound  
1: able to get out of bed/chair but does not go out  
2: goes out  
D | Neuropsychological problems  
0: severe dementia or depression  
1: mild dementia or depression  
2: no psychological problems  
E | Body Mass Index (BMI (weight in kg) / (height in m²))  
0: BMI < 19  
1: BMI = 19 to BMI < 21  
2: BMI = 21 to BMI < 23  
3: BMI = 23 and > 23  
F | Takes more than 3 medications per day  
0: yes  
1: no  
G | In comparison with other people of the same age, how does the patient consider his/her health status?  
0: not as good  
0.5: does not know  
1: as good  
2: better  
H | Age  
0: >85  
1: 80-85  
2: <80  
TOTAL SCORE | 0 - 17

**Impaired MGA if ≥ one abnormal questionnaire**

- **CIRS-G:** at least one grade ≥ 3
- **ADL:** score ≤ 5
- **IADL:** score ≤ 7
- **Timed Get up and Go:** > 20 s
- **MNA:** score ≤ 23,5
- **MMSE:** score ≤ 23
- **GDS-15:** score ≥ 6

**Setting:** Patients >70 with cancer

Pierre Soubeyran, Proc ASCO 2011
Results – Geriatric Assessment

• Duration of CGA 67.7 mn +/- 24.6

• Prevalence of abnormal MGA 80%
  – At least one abnormal questionnaire (Gold standard)
  – Questionnaire with missing question(s) considered abnormal

<table>
<thead>
<tr>
<th>1435 pts</th>
<th>Anormal</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADL</td>
<td>&lt;6</td>
<td>219</td>
<td>15.3</td>
</tr>
<tr>
<td>IADL</td>
<td>&lt;8</td>
<td>686</td>
<td>47.8</td>
</tr>
<tr>
<td>GDS15</td>
<td>≥6</td>
<td>457</td>
<td>32.1</td>
</tr>
<tr>
<td>MMS</td>
<td>&lt;24</td>
<td>292</td>
<td>20.3</td>
</tr>
<tr>
<td>MNA</td>
<td>≤23,5</td>
<td>627</td>
<td>43.7</td>
</tr>
<tr>
<td>Timed Get up &amp; Go</td>
<td>&gt;20 s</td>
<td>330</td>
<td>23</td>
</tr>
<tr>
<td>CIRS-G</td>
<td>Grade 3-4</td>
<td>602</td>
<td>41.9</td>
</tr>
</tbody>
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Pierre Soubeyran, Proc ASCO 2011
CGA is time-consuming: screening tools

Gold standard: Impaired Multidimensional Geriatric Assessment (MGA)

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2 : no decrease in food intake  
0 : weight loss > 3 kg |
| Age                                                                  | 0 : ≥85  
1 : 80-85  
2 : <80 |
| TOTAL SCORE                                                          | 0 - 17 |

Impaired MGA if ≥ one abnormal questionnaire

<table>
<thead>
<tr>
<th></th>
<th>Se</th>
<th>Sp</th>
<th>PPV</th>
<th>NPV</th>
<th>K</th>
<th>Time (mn)</th>
</tr>
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<tbody>
<tr>
<td>G8</td>
<td>76.6% (74-79)</td>
<td>64.4% (58.6-70)</td>
<td>89.6% (87.6-91.5)</td>
<td>40.7% (36.1-45.4)</td>
<td>0.65</td>
<td>4.4 +/- 2.9</td>
</tr>
<tr>
<td>VES13</td>
<td>68.7% (65.9-71.4)</td>
<td>74.3% (68.8-79.3)</td>
<td>91.5% (89.4-93.3)</td>
<td>37.1% (33.2-41.3)</td>
<td>0.64</td>
<td>4.3 +/- 4.6</td>
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Setting: Patients >70 with cancer

Pierre Soubeyran, Proc ASCO 2011
CGA is time-consuming: screening tools

### Gold standard: Impaired Multidimensional Geriatric Assessment (MGA)

<table>
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<tr>
<th>Items</th>
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</table>
| A     | Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties? | 0 : severe decrease in food intake  
1 : moderate decrease in food intake  
2 : no decrease in food intake  
0 : weight loss > 3 kg |
| B     | Weight loss > 3 kg |
| C     | Mobility (hpus) |
| E     | No |
| F     | Basic (hpus) |
| H     | Tars |
| P     | Imp | Se | Sp | PPV | NPV | K | Time (mn) |
| G8    | 76.6% (74-79) | 64.4% (58.6-70) | 89.6% (87.6-91.5) | 40.7% (36.1-45.4) | 0.65 | 4.4 +/- 2.9 |
| VES13 | 68.7% (65.9-71.4) | 74.3% (68.8-79.3) | 91.5% (89.4-93.3) | 37.1% (33.2-41.3) | 0.64 | 4.3 +/- 4.6 |

CGA is useful  
And screening is feasible

### Setting: Patients >70 with cancer

Impaired MGA if ≥ one abnormal questionnaire

Pierre Soubeyran, Proc ASCO 2011
How to organize?

Standard Management

G8 Screening

Evaluation and cautious management

> 14

≤ 14
How to organize?

- **G8 Screening**
  - >14
  - ≤ 14

- **Selection procedure**
  - MGA ? CGA ? Other ?

- **Cautious Management**
  - Oncologist + Geriatrician

- **Standard Management**

- **Management**
How to organize?

The French UCOG model

- Geriatric Oncology Coordinating Units
  - 15 already created since 2006
  - A few more to be accredited soon

- Main goals of the UCOG in each region
  - Organize cancer care for older patients
  - Participate to teaching and training
  - Perform research in the geriatric oncology field
  - Inform patients and public
Lessons learned - 1

• To promote geriatric oncology, we have to convince colleagues with evidence-based data

• Design of experimental arms should be feasible in the daily practice
  – Technically and in terms of health professionals

• Patients included should be close to the reality
  – Participation of community hospitals and private practice

• Community hospitals should be involved from the beginning of research
  – Implementation in daily practice
Lessons learned - 2

- Begin with transversal research
- Then refine tools in each cancer type
Finally

• Still a lot to do!
• When to propose geriatric intervention?
• How to take advantage of biological specificities?
Acknowledgments

Investigateurs ONCODAGE
Patients