Update of the clinical trials for the elderly

European / EORTC Perspective

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Situation in Europe:

• Typical 1 in 4 societies -> 25% of the population will be 65+ in 2020

• Typical age dependent increase in incidence and mortality rates in cancer

• Different health care and research structure in every single nation
Structure

• Differences in incidence-, mortality- and 5 years survival rates
• How to approach the elderly cancer patients in trials
• Approaches in different European Countries
• EORTC activities
• Future steps
EUROCARE: Age-standardised 5 years survival rates in %

- Schweden*
- Island
- Schweiz*
- Österreich*
- Frankreich*
- Deutschland*
- Finnland
- Spanien*
- Niederlande*
- Europa*
- Italien*
- Dänemark
- England*
- Slowakei
- Schottland
- Slowenien
- Estland
- Polen*
What is the appropriate research strategy to approach the elderly patient?

- no upper numerical age limit

  or

  specially designed trials for elderly patients?
What is the appropriate research strategy to approach the elderly patient?

North Central Cancer Treatment Group Experience

Table 1. Salient Trial Eligibility Criteria and Characteristics

<table>
<thead>
<tr>
<th></th>
<th>N9921 (elderly-specific trial)</th>
<th>N0022 (elderly-specific trial)</th>
<th>98-24-52 (age-unspecified trial)</th>
<th>N0026 (age-unspecified trial)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total accrual, No. of patients</td>
<td>50</td>
<td>58</td>
<td>106</td>
<td>157</td>
</tr>
<tr>
<td>No. of patients &gt; 65 years</td>
<td>50</td>
<td>58</td>
<td>43</td>
<td>75</td>
</tr>
<tr>
<td>Tumor stage</td>
<td>IV or recurrent cancer or unresectable cancer</td>
<td>IV or recurrent cancer or unresectable cancer</td>
<td>IIIB or IV</td>
<td>IV or recurrent cancer or IIIB (in patients who are not candidates for combined modality therapy)</td>
</tr>
<tr>
<td>performance score (Eastern Cooperative Oncology Group)</td>
<td>0, 1, 2</td>
<td>0, 1, 2</td>
<td>0, 1</td>
<td>0, 1</td>
</tr>
<tr>
<td>Age restriction</td>
<td>≥ 65</td>
<td>≥ 65</td>
<td>≥ 10</td>
<td>≥ 10</td>
</tr>
</tbody>
</table>

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What is the appropriate research strategy to approach the elderly patient?

**Table 3. Baseline Characteristics of Elderly-Specific and Age-Unspecified Trials**

<table>
<thead>
<tr>
<th></th>
<th>Age-Unspecified (n = 118)</th>
<th>Elderly-Specific (n = 108)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>70</td>
<td>66.1%</td>
<td>73</td>
</tr>
<tr>
<td>Range</td>
<td>65-85</td>
<td></td>
<td>65-87</td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>26.7</td>
<td></td>
<td>25.8</td>
</tr>
<tr>
<td>Range</td>
<td>15.5-43.9</td>
<td></td>
<td>16.5-41.6</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>39</td>
<td>33%</td>
<td>38</td>
</tr>
<tr>
<td>Male</td>
<td>79</td>
<td>67%</td>
<td>70</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>106</td>
<td>93%</td>
<td>104</td>
</tr>
<tr>
<td>Nonwhite</td>
<td>8</td>
<td>7%</td>
<td>3</td>
</tr>
<tr>
<td>Performance score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>45</td>
<td>38%</td>
<td>32</td>
</tr>
<tr>
<td>1</td>
<td>73</td>
<td>62%</td>
<td>57</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0%</td>
<td>19</td>
</tr>
<tr>
<td>Stage group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIIIB</td>
<td>12</td>
<td>16%</td>
<td>17</td>
</tr>
<tr>
<td>IV</td>
<td>62</td>
<td>84%</td>
<td>80</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0%</td>
<td>2</td>
</tr>
</tbody>
</table>

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Median survival time:
302 days (age-unspec.) vs. 232 days (elderly-spec)

No difference after adjustment for:
- Age,
- ECOG-PS,
- Stage, and
- BMI

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Table 4. Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>Age-Unspecified (n = 118)</th>
<th>Elderly-Specific (n = 104)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with any grade 3+ event</td>
<td>112</td>
<td>63</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Patients with any grade 3+ hematologic event</td>
<td>80</td>
<td>10</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Patients with any grade 3+ nonhematologic event</td>
<td>95</td>
<td>59</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Patients with grade 3+ neutropenia</td>
<td>66</td>
<td>9</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Patients with grade 3+ dyspnea</td>
<td>21</td>
<td>18</td>
<td>.78</td>
</tr>
<tr>
<td>Patients with grade 3+ fatigue</td>
<td>30</td>
<td>9</td>
<td>.001</td>
</tr>
<tr>
<td>Patients with grade 3+ leukopenia</td>
<td>47</td>
<td>2</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Patients with grade 3+ thrombocytopenia</td>
<td>16</td>
<td>1</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Patients with grade 3+ febrile neutropenia</td>
<td>15</td>
<td>1</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

NOTE. Throughout Table, adverse events are included only if their frequency was ≥ 10% in either group.
Trials in Europe

- Disease orientated trial groups develop a focus on elderly patients
- National trials groups develop a focus on elderly cancer patients
- European trials groups develop a focus on elderly cancer patients
National Trial Groups

Disease orientated trial groups which develop a focus on elderly patients, e.g. Diffuse large B-cell lymphoma:

- **GELA**: CHOP-21 vs. R-CHOP-21,
- **DSHNHL**: CHOP-21 vs. CHOP-14 + G-CSF
  CHOP-14 vs. R-CHOP-14 + G-CSF
- ...
Phase II – III trials in lung cancer, breast cancer, colo-rectal cancer, cancer of the ovary and
Trials on communication and decision making

www.gioger.org
National Trial Groups: French – GERICO Trial

Phase II trials
- GERICO-2: Advanced colorectal cancer
  Capecitabine + Oxaliplatin - finished
- GERICO-3: Radiotherapy in Breast Cancer – inclusion completed
- GERICO-4: Advanced breast cancer
  Docetaxel every 15 day stopped early based on toxicity – Poster at SIOG 2008 V. Girré
- GERICO-5: Advanced lung cancer
  Docetaxel every 15 day - closed
- GERICO-6: Adjuvant breast cancer, ER-
  Myocet + Cyclophosphamid – presented as oral present. at SIOG 2008 V. Girré

Projects:
- GERICO-8: 1st line metastatic CRC in planning Beginning 2009
- GERICO-9: Lapatinib after Trastuzumab in planning Beginning 2009
- GERICO-10: Prostate?
National Trial Groups: Germany –

Breast Cancer: Adjuvant Tx - ICE Trial
Lung Cancer: Randomised Phase III trials

Initiative Geriatric Haematology and Oncology (IN-GHO®):
- www based registry
- patients aged 70+ with cancer
- CGA at baseline and follow up after 2-3 and after 6 months
- Planed accrual of 2000 – 3000 patients
## Breast Cancer: Current trials on adjuvant Chemotherapy

<table>
<thead>
<tr>
<th>Trial / Group</th>
<th>Population</th>
<th>Inclusion criteria</th>
<th>Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICE</td>
<td>≥ 65</td>
<td>N1-3 or N0 and T &gt; 2 cm or G ≥ I, or HR-</td>
<td>NIL vs. Capecitabine and all patients receive iv or oral Ibandronate; all HR + pts receive an AI</td>
</tr>
<tr>
<td>CALGB-Intergroup 49907</td>
<td>&gt; 65</td>
<td>T1-4 (tumor size ≥ 1 cm), N0, M0 or T1-4, N1-3, M0 HR + or -</td>
<td>AC or* CMF vs. Capecitabine</td>
</tr>
</tbody>
</table>
| CASA / IBCSG 32-05 / BIG 1-05    | > 65       | HR -                                                                                | Option 1: liposomal doxorubicin vs. NIL  
Option 2: liposomal doxorubicin vs. metronomic (CM)                                        |
| ACTION                           | > 70       | Uncertain indication for chemotherapy                                               | Randomisation 1: CTX vs. NIL  
Randomisation 2: AC or EC 4 x every 3 or every 2 weeks + pegylated G-CSF                    |
Breast Cancer trials: Adjuvant CTX

- **ICE trial:**
  - recruitment finished
  - results not yet available
  - ICE-2 trial in planning

- **ACTION trial:**
  - ongoing

- **CASA trial:**
  - poor recruitment -> closed
European Organisation for Research and treatment of Cancer (EORTC)

- The aims of the EORTC are to develop, conduct, coordinate, and stimulate translational and clinical research in Europe to improve the management of cancer and related problems by increasing survival but also patients’ quality of life.

- Extensive and comprehensive research in this wide field is often beyond the means of individual European laboratories and hospitals, and can best be accomplished through the multidisciplinary multinational efforts of translational research scientists and clinicians.

- Further clinical progress in cancer treatment will be accomplished mainly through the conduct of translational research projects, efficient drug development and the execution of large, prospective, randomized, multicenter cancer clinical trials.

- The ultimate goal of the EORTC is to improve the standard of cancer treatment in Europe, through the evaluation of innovative drugs, and to establish more effective therapeutic strategies, using drugs already commercially available, or surgery and radiotherapy.

www.eortc.be
The organisation was founded as an international organisation under Belgian law in 1962 by eminent oncologists working in the main cancer research institutes of the EU countries and Switzerland. It was named Groupe Européen de Chimiothérapie Anticancéreuse (GECA), and became the European Organisation for Research and Treatment of Cancer (EORTC) in 1968.
EORTC – Task Force Cancer in the Elderly

- EORTC established a Task Force „Cancer in the Elderly“ in the Nineties of the last Century
- Chairman: Ian Fentiman, UK; Matti Aapro, Ch;
- Mainly advisory function
EORTC – Task Force Cancer in the Elderly

- Currently two protocols with disease orientated groups in preparation:
  - patients with advanced breast cancer
  - patients with advanced colorectal cancer
- Suggestion of an geriatric screening for every patient aged 70+, who is included in an EORTC trial
EORTC – Task Force Cancer in the Elderly

- Evaluation of an elderly specific quality of life questionnaire together with the QoL group
- Evaluation of the existing EORTC data base regarding elderly specific questions
Conclusions

• EORTC mainly works through disease orientated groups
• Poor men power in the Task Force to have a member in every disease orientated group
• No active trials so far – necessary to form a group
• Focus on translational research