Latest Achievements in the Care of Older Adults:
Medical Oncology

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Director of the Cancer and Aging Research Program
City of Hope
Overview

To prepare for this talk:

- Medline search: Terms “geriatric oncology”
- Reviewed table of contents of journals with the highest impact factor for articles in “cancer and aging”
- Limit to articles published in 2006-2007
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Good news! Too many articles to discuss!
Overview

Chose articles:

- Built on previous work
- Focus on data from 3 major tumor types
- Challenges in geriatric oncology
- Achievements in the field of geriatric oncology
Breast Cancer
## Poly-Chemotherapy for Early Breast Cancer

<table>
<thead>
<tr>
<th>Age</th>
<th>Recurrence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>40% (SD 6)</td>
<td>29% (SD 7)</td>
</tr>
<tr>
<td>40-49</td>
<td>36% (SD 4)</td>
<td>30% (SD 5)</td>
</tr>
<tr>
<td>50-59</td>
<td>23% (SD 3)</td>
<td>15% (SD 4)</td>
</tr>
<tr>
<td>60-69</td>
<td>13% (SD 3)</td>
<td>9% (SD 4)</td>
</tr>
<tr>
<td>≥70</td>
<td>12% (SD 11)</td>
<td>13% (SD 12)</td>
</tr>
</tbody>
</table>

*EBCTCG; Lancet 2005: 365: 1687-171*
Only 1224 women > age 70

“These trials of chemotherapy involved too few women older than 70 years of age to be reliably informative as to whether it confers any net survival benefit among them.”

EBCTCG; Lancet 2005: 365: 1687-171
Use and Outcomes of Adjuvant Chemo in Older Women with Breast Cancer

- SEER Database Study 1991 to 1999
- Cox Regression for BC Survival and Overall Survival for chemo vs not

<table>
<thead>
<tr>
<th>LN (+)</th>
<th>Breast CA Survival</th>
<th>Overall Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>ER (-)</td>
<td>0.72</td>
<td>0.54-0.96</td>
</tr>
<tr>
<td>ER (+)</td>
<td>1.05</td>
<td>0.85-1.31</td>
</tr>
</tbody>
</table>

Giordano et al. JCO 2006
Do Older Women with ER Negative Disease Benefit From Chemotherapy?

- SEER Database Study 1992 to 2002
- Stage I – III
- Age 66 and older
- 5,081 patients
- 34% treated with chemotherapy
- Chemotherapy associated with a 16% reduction in mortality

Elkin, Hurria et al. JCO 2006
Benefit vs Risk Ratio of Adjuvant Chemotherapy
Chemotherapy Toxicity in Older Patients

- Node (+) BC enrolled in 3 CALGB/CTSU trials
  - 8541: comparison of CAF in 3 dose schedules
  - 9344: AC +/- paclitaxel
  - 9741: AC-T or ATC q2 vs q3 weeks

- Toxicity data from 6174 of 6642 pts (93%)

- Low representation of older patients on clinical trials
  - 7% > age 65
  - 3% > age 70

*Muss et al, JCO 2007*
# Increased Toxicity in Older Patients

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt;50</th>
<th>50-64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML</td>
<td>0.3%</td>
<td>0.7%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Discontinue Tx</td>
<td>3%</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>Death (%)</td>
<td>0.2%</td>
<td>0.4%</td>
<td>1.5%</td>
</tr>
<tr>
<td>AML (N)</td>
<td>1</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Cardiac (N)</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Other (N)</td>
<td>2</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

Multivariate analysis: Older pts ↑ risk of Gr 4 heme tox

*Muss et al, JCO 2007*
AML after Adjuvant Chemo in Pts > 65

- 64,715 pts: 15.7% received chemo
- Median age 75.6

<table>
<thead>
<tr>
<th>Risk of developing AML at 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy vs not</td>
</tr>
</tbody>
</table>

- Multivariate analysis:
  - Increased age associated with increased risk
  - Type of chemo or GCSF use in 1st yr did not increase risk

*Patt et al, JCO 2007*
CHF after Adjuvant Chemo in Pts > 65

- 43,338 pts age 66-80
- Age 66-70:
  - ↑ risk of CHF treated with anthracycline
  - HR 1.25 (95% CI 1.12 to 1.42)
- Age 71-80:
  - No increased risk based on chemo type
- Predictors of CHF:
  - age, black race, trastuzumab tx, DM, HTN, CAD

Pinder et al, JCO 2007
Adjuvant Trial for Older Patients
CALGB-CTSU 49907 (PI: H. Muss, MD)

Randomize

65 and older
≥ 1 cm and any N
Hormonal Rx per MD
Companion Trials
QOL, compliance and tumor biology

CMF x 6 or
AC x 4

Capecitabine x 6
## Adjuvant Treatment of BC in Older Adults: Randomized Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>Arms</th>
<th>Eligibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASA IBCSG BIG 1-05</td>
<td>1296</td>
<td>Low dose CM vs Liposomal doxorubicin vs Observation</td>
<td>Age &gt; 65, ER/PR &lt;10%</td>
</tr>
<tr>
<td>ICE GBG 32</td>
<td>1500</td>
<td>Ibrandronate vs Ibandronate + Capecitabine</td>
<td>Age &gt; 65, Any receptor</td>
</tr>
<tr>
<td>ELDA</td>
<td>300</td>
<td>IV CMF vs Docetaxel</td>
<td>Age 65 to 80, Any receptor</td>
</tr>
</tbody>
</table>
Lung Cancer
Non-Small Cell Lung Cancer
5-Year Survival by Age

## Advanced NSCLC in Older Adults: Randomized Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>Arms</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELVIS</td>
<td>154</td>
<td>Vinorelbine vs BSC</td>
<td>Vinorelbine improves 1-yr survival</td>
</tr>
<tr>
<td>SICOG</td>
<td>120</td>
<td>Vinorelbine vs Vinorelbine + Gemcitabine</td>
<td>Combo improves median survival</td>
</tr>
<tr>
<td>MILES</td>
<td>698</td>
<td>Vinorelbine vs Gemcitabine vs Vinorelbine + Gemcitabine</td>
<td>No improvement in PFS or OS with combo</td>
</tr>
</tbody>
</table>

Randomized Trials for Advanced NSCLC in Older Patients

Take home messages:

- Single agent chemo better than best supportive care
- Conflicting results regarding the benefits of combination chemo
- No trial evaluated a platinum or taxane combination
Cisplatin Combos for Lung CA in Older Adults: Miles 2P

Lung Cancer
Stage IIIB or IV
Phase I/II

Cisplatin + Gemcitabine
Cisplatin + Vinorelbine

Feasible Doses:
cisplatin 40 mg/m² + vinorelbine 25 mg/m² D1, D8
cisplatin 60 mg/m² + gemcitabine 1000 mg/m² D1, D8

Gridelli et al, JCO 2007
Cisplatin Combos for Lung CA in Older Adults: Next Steps

Lung Cancer
Stage IIIB or IV
Phase III

Cisplatin + Gemcitabine

Dosing:

cisplatin 60 mg/m² day 1
gemcitabine 1000mg/m² D 1 and 8
cycle repeated every 3 week

Gridelli et al, JCO 2007
Adjuvant Chemo for Lung CA in Older Adults

JBR 10 Trial
Lung CA: Stage IB or II
482 pts (155 > age 65)

Adjuvant Cisplatin + Vinorelbine
No Adjuvant Therapy

Results:
- Despite older adults receiving less chemo....
- Chemo *improves OS* in older adults
  (HR 0.61; 95% CI 0.38 –0.98; p=0.04)
- No age related difference in toxicity

*Pepe et al, JCO 2007*
Colon Cancer
FOLFOX4 in Older Adults

- Pooled analysis of 4 clinical trials of FOLFOX4
- 3742 pts with colorectal CA
- 16% > age 70

No significant difference in dose intensity, PFS, or OS by age

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Age &lt; 70</th>
<th>Age ≥ 70</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade &gt; 3 neutropenia</td>
<td>43%</td>
<td>49%</td>
<td>.04</td>
</tr>
<tr>
<td>Grade &gt; 3 platelets</td>
<td>2%</td>
<td>5%</td>
<td>.04</td>
</tr>
</tbody>
</table>

Goldberg et al. JCO 2006
Colon Cancer:
Impact of Comorbidity on Survival

% 5 yr survival

Gross et al, JAGS 2006
Bevacuzimab: Older Adults at Risk for Arterial Thromboembolic Events (ATEs)

- Pooled analysis of 5 randomized clinical trials
- 1745 pts with colon, breast, lung CA treated with bevacuzimab vs bevacuzimab + chemo

<table>
<thead>
<tr>
<th></th>
<th>Bevacuzimab (N=782)</th>
<th>Bev + Chemo (N=963)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall incidence of ATE</td>
<td>1.7%</td>
<td>3.8%</td>
</tr>
<tr>
<td>Age ≥ 65</td>
<td>2.5%</td>
<td>7.1%</td>
</tr>
<tr>
<td>H/o prior ATE</td>
<td>3.4%</td>
<td>15.7%</td>
</tr>
<tr>
<td>Age ≥ 65 + h/o prior ATE</td>
<td>2.2%</td>
<td>17.9%</td>
</tr>
</tbody>
</table>

Scappaticci et al, JNCI 2007
Challenges in Geriatric Oncology:

1) Establishing Models of Geri-Onc Care

2) Accruing Older Adults to Randomized Phase III Studies
Survey of 216 SIOG members: 27% (N=58) responded
- 12 from USA/Canada and 42 from Europe
- All respondents identified geri-onc as their specialty
- 36% (N=21) had a Geri-Onc Program
- 85% oncology and 15% in geriatrics dept

Clinical trials
- 60% willing to enroll adults > age 70
- Less than 20% on trial

Monfardini et al. CROH 2007
Models of Care: Oncology-Acute Care for Elders Unit

- Novel Oncology-ACE Unit for pts age 65+ with cancer

**Interdisciplinary team**
- Geriatrician
- CNS
- Dietician
- PT/OT
- Case manager
- Social work
- Home health
- Hospice

**Team rounds: focus on GA domains**
- Screen for geriatric syndromes
- Communicate recommendations to primary MD

_Flood et al, JCO 2007_
Models of Care: 
Oncology-Acute Care for Elders Unit

- N=119

<table>
<thead>
<tr>
<th>Problems Identified</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dependent in ADL</td>
<td>45</td>
</tr>
<tr>
<td>Dependent in IADL</td>
<td>75</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>30</td>
</tr>
<tr>
<td>Depression</td>
<td>20</td>
</tr>
<tr>
<td>Weight loss</td>
<td>35</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interventions</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Tx</td>
<td>69</td>
</tr>
<tr>
<td>Occupational Tx</td>
<td>57</td>
</tr>
<tr>
<td>Nutrition consult</td>
<td>57</td>
</tr>
<tr>
<td>Home Health</td>
<td>30</td>
</tr>
<tr>
<td>Hospice</td>
<td>31</td>
</tr>
</tbody>
</table>

Flood et al, JCO 2007
Need to Improve Accrual of Older Adult to Phase III Trials

- 345 consecutive randomized phase III trials (1955-2000)
- 5 NCI sponsored cooperative groups

Only 1 exclusively enrolled pts age 65+:

57% no stratification by age

4% of trials (N=15) enrolled > 40% of pts age 65+:
- OS & EFS favored the innovative arm
- Treatment related mortality was similar

Kumar et al. JCO 2007
Understanding the Attitudes of Older Adults to Enrolling on Clinical Trials

- Self-administered questionnaire (N=94)
- Interviews (N=17)

3/4th willing to participate in a clinical trial

Factors most likely to influence willingness to participate:
- MD recommendation
- Potential for treatment to make them feel better

Townsley et al, BMC Cancer 2006
Barriers to Participation of Older Women with Breast Cancer in Clinical Trials

<table>
<thead>
<tr>
<th></th>
<th>&lt;65yo</th>
<th>65+yo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offered trial</td>
<td>51%</td>
<td>35%</td>
</tr>
<tr>
<td>Offered and accepted</td>
<td>56%</td>
<td>50%</td>
</tr>
</tbody>
</table>

- Multivariate analysis: Age only predictor factor of whether patient offered clinical trial
- Controlling for race, comorbidity, functional status

*Kemeny MN et al, JCO 2003*
Clinical Trials and the Older Patient
Barriers to Participation

- Top reasons why MD not offer protocol

**Young**
- not best therapy
- not aware it was open
- not eligible

**Old**
- not best therapy
- not aware it was open
- too toxic

*Kemeny MN et al, JCO 2003*
Same Chronological Age; Different Functional Age

Do we have a clinical trial available for both?
Achievements in Geriatric Oncology
Renal Insufficiency in Elderly Cancer Patients


Chemotherapy in Older Patients

Lichtman et al. JCO 2007

Use of Bisphosphonates in Older Adults

Body et al. European J of Cancer 2007
SIOG Geriatric Oncology Guidelines

- Organization of Clinical Activity in Geriatric Oncology
  Monfardini et al. CROH 2007

- The Illness Trajectory of Elderly Cancer Patients across Cultures

- The Use of CGA in Older Cancer Patients
  Extermann et al. CROH 2005
1st Special Series Dedicated to Geriatric Oncology

Co-editors:
S. Lichtman, MD
L. Balducci, MD
M. Aapro, MD
B.J. Kennedy Award for Scientific Excellence in Geriatric Oncology
Geriatric Oncology

Science

Art