Chemotherapy and Toxicity Assessment

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Chronological Age ≠ Functional Age

Age 80
Older adults are at risk for cancer therapy toxicity

Muss et al., Journal of the American Medical Association 2005
Muss et al., Journal of Clinical Oncology 2007
Cassidy et al., Journal of Cancer Research and Clinical Oncology 2010
Rocha Lima et al., Cancer 2002
Argiris et al., Journal of Clinical Oncology 2004
Hurria et al., Journal of Clinical Oncology 2011
Folprecht et al., Annals of Oncology 2011
Goldstone et al., Blood 2001
Machtay et al., Journal of Clinical Oncology 2008
Zauderer et al., Journal of Geriatric Oncology 2013
Quoix et al., Lancet 2011
Schild et al., Journal of Clinical Oncology 2003
Zhu et al., Journal of the American Medical Association 2012
Machtay et al., Journal of Clinical Oncology 2008
Crivellari et al., Journal of Clinical Oncology 2000
Pinder et al., Journal of Clinical Oncology 2007
Can We Anticipate the Toxicity?

Geriatric Assessment:
Identifying the Older Adult at Risk for Treatment Toxicity and Intervening
What is old?

65
Understanding the Gray

Factors other than chronological age that predict morbidity & mortality in older adults

- Functional status
- Comorbid medical conditions
- Nutritional status
- Cognition
- Psychological state
- Social support
- Medications (polypharmacy)

Geriatric Assessment
SIOG Practice Guidelines

PRACTICE GUIDELINE

Comprehensive Geriatric Assessment (CGA) in oncological patients

Version: 20 July 2011

This guideline was established under the auspices of the educational committee of SIOG. The guidelines are available at the SIOG website, and are meant to become an 'uptodate' system where health care workers can add new evidence or information if required. All information or questions can be addressed to SIOG at the email address siog@genolier.net

Concept: Cindy Kenis and Hans Wildiers

Coworkers: Ulrich Wedding, Martine Extermann, Koen Milisen, Johan Flamaing

www.sio.org
Can Geriatric Assessment Predict Chemo Toxicity? (CARG)

Eligibility criteria:
- Age 65 or older
- Diagnosis of cancer
- To start a new chemotherapy regimen

**Timepoint 1:**
- Pre-chemo Geriatric Assessment

**Timepoint 2:**
- Post-chemo Geriatric Assessment
- Chemotherapy: toxicity grading at each visit

- Sample size: 500 patients (Chemo alone)
- 7 participating institutions (Cancer and Aging Research Group)

*Hurria et al, JCO 2011*
Predictors of Toxicity

- Age ≥ 72 years
- GI/GU Cancer
- Standard Dose
- Polychemotherapy
- Hemoglobin (male: <11, female: <10)
- Creatinine Clearance (Jelliffe-ideal wt <34)
- Fall(s) in last 6 months
- Hearing impairment (fair or worse)
- Limited in walking 1 block (MOS)
- Assistance required in medication intake (IADL)
- Decreased social activity (MOS)

Age
Tumor/Treatment
Variables

Labs

Geriatric
Assessment
Variables

Hurria et al, JCO 2011
Risk of Toxicity by Score

- Low (30%)
  - 0-3: 25%
  - 4-5: 32%
- Medium (52%)
  - 6-7: 50%
  - 8-9: 54%
- High (83%)
  - 10-11: 77%
  - 12-19: 89%

Total Risk Score

Hurria et al, JCO 2011
MD-rated KPS vs. Predictive Model

Chi-square test $p=0.19$

Chi-square test $p<0.0001$

Hurria et al, JCO 2011
Next Steps

- All Tumor Types: Validated Model
  - N=250; Completed Accrual

- Disease-Specific
  - Breast: Adjuvant Therapy (Dr. Hurria)
  - Ovarian: First Line Age ≥ 70 (Dr. VonGreunigan)
  - Breast: Endocrine Therapy +/- Bevacuzimab (Dr. Dickler)
  - Breast: Taxanes in Metastatic Breast Cancer (Dr. Rugo)
  - AML: First Line Age ≥ 60 (Dr. Klepin/Dr. Ritchie)
  - CLL: First Line Age ≥ 65 (Dr. Woyach)
  - GI: First Line Age ≥ 75 (Dr. McCleary)
Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) Score

- Prospective multicentric study
- 518 patients age $\geq 70$ yrs

<table>
<thead>
<tr>
<th>Predictors of Toxicity</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Heme</td>
<td></td>
</tr>
<tr>
<td>Diastolic Blood Pressure</td>
<td>$\leq 72$</td>
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<tr>
<td>IADL</td>
<td>26-29</td>
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<tr>
<td>Lactate Dehydrogenase</td>
<td>0-459</td>
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<tr>
<td><strong>Chemotherapy Toxicity</strong></td>
<td>0-0.44</td>
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<tr>
<td>Non-Heme</td>
<td></td>
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<tr>
<td>ECOG PS</td>
<td>0</td>
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<tr>
<td>Mini Mental Health Status</td>
<td>30</td>
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<tr>
<td>Mini Nutritional Assessment</td>
<td>28-30</td>
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<tr>
<td><strong>Chemotherapy Toxicity</strong></td>
<td>0-0.44</td>
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</tbody>
</table>

Extermann et al, Cancer 2012
CRASH Model

Extermann et al, Cancer 2012
Phase III Study:
Age $\geq 75$
Metastatic Colorectal Cancer
1\textsuperscript{st} line

Randomize

N=62
FU-Based Chemotherapy Alone
Mean Age: 80.3

N=61
FU-Based Chemotherapy + Irinotecan
Mean Age: 80.5

All underwent a Geriatric Assessment

Aparicio et al., J Clin Oncol, 2013
## Predictors of Toxicity & Dose Modification

<table>
<thead>
<tr>
<th>Grade 3-4 Toxicity</th>
<th>OR (95% CI)</th>
<th>P-Value</th>
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<tbody>
<tr>
<td>Irinotecan Arm</td>
<td>5.03 (1.61-15.77)</td>
<td>.006</td>
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<tr>
<td>Mini-Mental State Examination (MMSE) ≤ 27/30</td>
<td>3.84 (1.24-11.84)</td>
<td>.019</td>
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<tr>
<td>Impaired Autonomy (IADL)</td>
<td>4.67 (1.42-15.32)</td>
<td>.011</td>
</tr>
</tbody>
</table>

Cognitive & physical function should be considered when making treatment decisions.

Aparicio et al., J Clin Oncol, 2013
The Past:
Risk Factors for Chemotherapy Toxicity

- Patient Factors
  - Age
  - ECOG PS/KPS
  - Labs

- Tumor and Treatment Factors
  - Cancer Type
  - Chemotherapy
### The Present: Geriatric Assessment Items Predictive of Chemotherapy Toxicity

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Aaldriks</th>
<th>Aparicio</th>
<th>Extermann</th>
<th>Freyer</th>
<th>Hurria</th>
<th>Kanesvaran</th>
<th>Soubeyran</th>
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</thead>
<tbody>
<tr>
<td>Daily Activities (ADL &amp; IADLs)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
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<tr>
<td>Hearing (Fair or Deaf)</td>
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<td></td>
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<td>x</td>
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<td>Nutrition</td>
<td>x</td>
<td></td>
<td>x</td>
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<tr>
<td>Cognition</td>
<td>x</td>
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<td>x</td>
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<td>x</td>
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<tr>
<td>Psychological Status</td>
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<td>Social Activities</td>
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<td></td>
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<td>x</td>
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</tbody>
</table>

*Aaldriks et al, Crit Rev Oncol Hematol 2011  
Papiricio et al, J Clin Oncol 2013  
Extermann et al, Cancer 2012  
Freyer et al, Annals of Oncology 2005  
Hurria et al, J Clin Oncol 2011  
Kanesvaran et al, J Clin Oncol 2011  
Soubeyran et al, J Clin Oncol 2012*
Benefits of Geriatric Assessment in Older Patients with Cancer

➢ Helps distinguish functional vs. chronological age
➢ Predicts toxicity to cancer treatment
➢ Uncover problems not detected by routine H&P

Leads to interventions guided by geriatric assessment results

Hurria et al. JCO 2011  
Repetto et al. JCO 2002  

Maione et al. JCO 2005  
Poon et al. JCO 2011  
Extermann et al. Cancer 2011
Next Steps

Integrating the Geriatric Assessment into Practice

Stay Tuned for the 4pm talk

“Communicating Treatment Options to Older Patients: Challenges and Opportunities”
Acknowledgements

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