Comprehensive Geriatric Assessment (CGA) in Older Patients with Malignant Hemopathies

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• **Why CGA?**
  - Malignancies incidence increase in older pts
  - Hematologic malignancies remain Curable in older pts!
  - Chronological Age does not mean anything!

• **When CGA?**
  - All patients above 70-75y?
  - As soon as a treatment is required

• **How CGA?**
  - Optimal Tools?
  - Geriatricians? Onco-geria-nurse? Hematologist?

→ **Which Results?***
The European Union population is ageing
\textbf{WHY} \\
\textbf{WHEN} \\
\textbf{HOW}

\begin{itemize}
  \item \textbf{Cancer is a disease of the elderly}
\end{itemize}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{chart.png}
\caption{Incidence and Mortality of Various Cancers by Age Group.}
\end{figure}

\textit{NHL} = non-Hodgkin's lymphoma

Hematologic malignancies

account for 10% of cancers and 7% of cancer mortality

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Median Age (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDS</td>
<td>75</td>
</tr>
<tr>
<td>AML</td>
<td>70</td>
</tr>
<tr>
<td>MM</td>
<td>70</td>
</tr>
<tr>
<td>NHL</td>
<td>67</td>
</tr>
<tr>
<td>CLL</td>
<td>72</td>
</tr>
</tbody>
</table>
• Chronological age does not mean anything!
• Poor marrow, renal, neurological... Tolerance

• Comorbidities (= polymedication)
• Geriatric syndromes (falls, cognitive troubles, incontinence, dementia, dependance)

• Socio-economical limitations
WHY

Haematopoietic reserve declines with age

- Mean ANC nadir, AC adjuvant therapy for breast cancer
  - <65 years, n=32
  - ≥65 years, n=11

- Dose delays >3 days
- Dose reductions ≥15%

WHEN

- Schwenkglenks et al. EBCC 2008:62
- Aapro et al. SABCS 2007:1088

HOW

Response to G-CSF is preserved in the elderly

- Dose-related response to filgrastim

- Patients %
  - Younger patients
    - Dose delays >3 days: 16%, dose reductions ≥15%: 23%
  - Elderly patients
    - Dose delays >3 days: 21%, dose reductions ≥15%: 29%

• Does your patient belong to the «Fit? Vulnerable? Unfit?» Group

• What’s the life expectancy of your patient?

• What’s life expectancy with the disease? Will the disease kill your patient?

• Does your patient want a treatment?
FUNCTIONALLY INDEPENDENT

GROUP 1

“Go-go”

Without comorbidity

standard cancer treatment

70-79 y = 75%
80-88 y = 20%
90+ y = 5%

GROUP 2

“Slow-go”

Intermediate frail patients

milder therapy, i.e. dose reduction

GROUP 3

“No-go”

Dependent in >1 ADL

>1 comorbidity

>1 geriatric syndrome

palliative treatment

Balducci, The Oncologist 2000
However, Clinical judgement is not reliable!

Physicians’ judgement and comprehensive geriatric assessment select different patients as fit for Chemotherapy (n=200)

<table>
<thead>
<tr>
<th></th>
<th>Fit patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jugement clinique</td>
<td>64.3%</td>
</tr>
<tr>
<td>CGA</td>
<td>26.5%</td>
</tr>
</tbody>
</table>

*Wedding U, Critical Reviews in Oncology/Hematology, 2007*
GERIATRIC SYNDROME

• Dependance
• Falls and trouble in walking
• Incontinence
• Denutrition
• Neglect and failure to thrive
• Cognitive function disturbances
• Dementia

→ Palliative care!
   = Palliation of symptoms
Impact of health status on life expectancy

To prolong survival? To cure?
Maintenance/improvement of quality of life?

- Neutropenic infection
- Anemia
- Mucositis
- Cardiotoxicity
- Neurotoxicity

=> Dependence
Dose-intensity and overall survival with R-CHOP?

- **WHY**
- **WHEN**
- **HOW**

![Graph showing survival rates over years post chemotherapy with different ARDI categories](image)

Estimated Survival vs. Years Post Chemotherapy

- ARDI: ≤85%
- ARDI: >85 to ≤90%
- ARDI: >90%

p = 0.002

Bosly 2007
Making treatment decisions in the older cancer patient

- 1st step: Patient
  - Comprehensive Geriatric Assessment
  - PS
- 2nd step: Tumour
  - Biological characteristics
  - Stage
  - Symptoms
- 3rd step: Goal
  - Quality of life?
  - Prolong survival?
- 4th step: Treatment choice
  - Active treatment
  - Supportive treatment
  - Palliative treatment
CGA: Comprehensive Geriatric Assessment

- **Functional evaluation**
  AGE, PS,
  Instrumental daily activity (IADL, ADL)

- **Physiological evaluation**
  Comorbid conditions,
  Weight, nutritional status

- **Psychological evaluation**
  Minimental status (MMS),
  Geriatric depression scale (GDS)

- **Socioeconomic evaluation**
  Income, Transportation, Family
ACTIVITIES OF DAILY LIVING

- continence
- grooming
- dressing
- feeding
- toileting
- transferring

Katz 1963
INSTRUMENTAL ADL
<table>
<thead>
<tr>
<th>TOOL (range)</th>
<th>SCORE</th>
<th>INTERPRETATION</th>
</tr>
</thead>
</table>
| ADL (6-24)  | - Dependent  
   - Independent  | - Score 7 – 24  
   - Score 6 |
| IADL (0-8)  | - Dependent  
   - Independent  | - Score 0 – 7  
   - Score 8 |
| MMSE (0-30) | - Normal  
   - Mild cognitive impairment  
   - Severe cognitive impairment | - Score ≥ 24  
   - Score 18 – 23  
   - Score ≤ 17 |
Influence of functionality and cognition

Time to death (months)

- Independent
- 1 ADL
- ≥ 2 ADL

OS

N = 9008
age ≥ 65y

*Vulnerable: need for assistance in ≥ 1 (or ≥ 2 if incontinence) activities of mobility or daily living or cognitive impairment without dementia or bowel + urinary incontinence

**Frail: need for assistance in ≥ 2 (or ≥ 3 if incontinence) activities of mobility or daily living or dementia or bowel + urinary incontinence

Rockwood K et al. Lancet 1999, 353, 205-206
<table>
<thead>
<tr>
<th>TOOL (range)</th>
<th>SCORE</th>
<th>INTERPRETATION</th>
</tr>
</thead>
</table>
| MNA-SF (0-14) | - Normal – not at risk  
- At risk for malnutrition  
- Malnourished | - Score 12 or more  
- Score 8 – 11  
- Score 0 - 7 |
| MNA (0-30) | - Normal – not at risk  
- At risk for malnutrition  
- Malnourished | - Score ≥ 24  
- Score from 17 to ≤ 23.5  
- Score < 17 |
| GDS (0-15) | - No depression  
- At risk for depression | - Score 0 – 4  
- Score ≥ 5 |
Influence of (Mal)nutrition

205 patients without cancer aged 75 years

# Charlson Comorbidity Index (CCI)

<table>
<thead>
<tr>
<th>Score</th>
<th>Condition</th>
</tr>
</thead>
</table>
| 1     | Myocardial infarction (history, not ECG changes only)  
Congestive heart failure  
Peripheral vascular disease (includes aortic aneurysm ≥6 cm)  
Cerebrovascular disease: CVA with mild or no residua or TIA  
Dementia  
Chronic pulmonary disease  
Connective tissue disease  
Pestic ulcer disease  
Mild liver disease (without portal hypertension, includes chronic hepatitis)  
Diabetes without end-organ damage (excludes diet-controlled alone) |
| 2     | Hemiplegia  
Moderate or severe renal disease  
Diabetes with end-organ damage (retinopathy, neuropathy, nephropathy, or brittle diabetes)  
Tumor without metastases (exclude if >5 y from diagnosis)  
Leukemia (acute or chronic)  
Lymphoma |
| 3     | Moderate or severe liver disease |
| 6     | Metastatic solid tumor  
AIDS (not just HIV positive) |

**NOTE.** For each decade > 40 years of age, a score of 1 is added to the above score.

Abbreviations: ECG, electrocardiogram; CVA, cerebrovascular accident; TIA, transient ischemic attack; AIDS, acquired immunodeficiency syndrome; HIV, human immunodeficiency virus.

Table from: http://nephron.org/cgi-bin/rpa_sdm.cgi, accessed March 13 2010
Distribution of comorbidity according to CCI

- diabetes without complications
- myocardial infarction
- second solid tumor
- ulcerative disease
- cerebrovascular disease
- connective tissue disease
- peripheral vascular disease
- diabetes with endorgan damage
- chronic pulmonary disease
- mild liver disease

Number of patients (n) = 60
CIRS: First investigated in elderly subjects (n=141) by Miller et al. 1992; used in modified version (CIRS-G) - predict survival and dependency

<table>
<thead>
<tr>
<th>Organ system</th>
<th>If illness/impairment present, please specify:</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ear/nose/throat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper gastrointestinal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower gastrointestinal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrine/metabolic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurological</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychiatric</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total Score: [ ] [ ]
CIRS: Should it be used in CLL patients?

GCLLSG CLL8 TRIAL FCR/FC; 2009 data set
Patients with CIRS 0-6

Goede et al., Oral presentation, EHA Annual Meeting 2012
WHY H-SCT – Sorror Comorbidity Index

WHEN

• A: grade 3-4 toxicity
• B: non-relapse mortality
• C: overall survival

WHY

ESAS
MNA
Falls
BFI
IADL
MUST
Barthel Index
ECOG-PS
GDS
CIRS

WHEN

EORTC Qlq-C30
SRH
TICS
Mini-COG
Clock drawing test

HOW

HADS
ADL
DOS
Karnofsky Index
MMSE
Charlson Index

MNA
ECOG-PS
<table>
<thead>
<tr>
<th>ITEM</th>
<th>POSSIBLE ANSWERS</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 loss of appetite  
1 = moderate loss of appetite  
2 = normal appetite |
| B Weight loss during the last 3 months?                              | 0 = weight loss >3kg  
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 (weight in kg/height in m²)                        | 0 = BMI less than 19  
1 = BMI 19 to less than 21  
2 = BMI 21 to less than 23  
3 = BMI 23 or greater |
| 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? | 0,0 = not as good  
0,5 = does not know  
1,0 = as good  
2,0 = better |
| Age                                                                 | 0 = >85  
1 = 80-85  
2 = <80 |

CHARACTERISTICS ASSOCIATED WITH MORTALITY AMONG ELDERLY PATIENTS WITH MALIGNANT HEMOPATHIES: COX REGRESSION

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Exp</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sociodemographic characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.117</td>
<td>1.022 to 1.221</td>
<td>0.015</td>
</tr>
<tr>
<td>Gender</td>
<td>2.499</td>
<td>0.962 to 6.491</td>
<td>0.060</td>
</tr>
<tr>
<td><strong>Disease-related characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Favorable Prognosis vs. Unfavorable Prognosis</td>
<td>7.168</td>
<td>2.654 to 19.361</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Full treatment choice vs. Dose reduction</td>
<td>1.536</td>
<td>0.557 to 4.236</td>
<td>0.407</td>
</tr>
<tr>
<td>Intolerance to treatment vs No intolerance</td>
<td>1.302</td>
<td>0.503 to 3.368</td>
<td>0.587</td>
</tr>
<tr>
<td><strong>Screening tool</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G8 test</td>
<td>1.129</td>
<td>0.928 to 1.374</td>
<td>0.225</td>
</tr>
<tr>
<td><strong>Comprehensive Geriatric Assessment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comprehensive Geriatric Assessment without Neuropsychological factors</td>
<td>1.228</td>
<td>0.860 to 1.753</td>
<td>0.259</td>
</tr>
<tr>
<td>Neuropsychological factors</td>
<td>3.560</td>
<td>1.130 to 11.210</td>
<td>0.030</td>
</tr>
</tbody>
</table>

St Dubruylle, 2014
Relevant points to consider before CLL treatment:

1. Does the patient require a treatment?
2. How «fit» is the patient?
3. Does the patient present high-risk features?
4. Does the patient want a treatment?

Ref: IWCLL guidelines - Hallek et al; BLOOD 2008
ESMO guidelines - Eichhorst et al; Ann Oncol 2010
Update on therapy - Gribben and O’Brien; J Clin Oncol 2011
FCR- Survival and Time to Fail (MDACC)

Descriptive statistics for each group (UD FCR)

<table>
<thead>
<tr>
<th>Group</th>
<th>No. uncst</th>
<th>N.censrd</th>
<th>Total N</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>52</td>
<td></td>
<td>134</td>
</tr>
<tr>
<td>2</td>
<td>29</td>
<td></td>
<td>73</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td></td>
<td>41</td>
</tr>
</tbody>
</table>

Pts. Died | Age
---|---
186 | <60
43 | 60-69
41 | >70

Courtesy of M.
**CLL8 : Hematological Toxicity according to ages**

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>FC treat</th>
<th>FC treat</th>
<th>P value</th>
<th>RFC</th>
<th>RFC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages</td>
<td>&lt; 70</td>
<td>&gt; 70 y</td>
<td></td>
<td>&lt; 70</td>
<td>&gt; 70 y</td>
<td></td>
</tr>
<tr>
<td>neutropenia</td>
<td>61</td>
<td>78</td>
<td>0.04</td>
<td>75</td>
<td>83</td>
<td>0.2</td>
</tr>
<tr>
<td>Febrile neutr</td>
<td>19</td>
<td>35</td>
<td>0.03</td>
<td>32</td>
<td>44</td>
<td>0.1</td>
</tr>
<tr>
<td>infections</td>
<td>0.7</td>
<td>5.4</td>
<td>0.02</td>
<td>1.9</td>
<td>4.7</td>
<td>0.1</td>
</tr>
</tbody>
</table>
Ibrutinib for 1\textsuperscript{st}-line and R/R CLL/SLL: (Byrd et al - #189, ASH 2013)

22-month PFS rate
- 1\textsuperscript{st}-line: 96%
- R/R (incl high risk): 76%

22-month OS rate
- 1\textsuperscript{st}-line: 96%
- R/R: 85%
- Median OS not reached

Safety: no evidence of cumulative toxicity
Therapeutical approach in older patients

- PATIENT Assessment
- Disease Characteristics
- PATIENT Quality of Life
« QUALITY »
of Life is
more important
than
« QUANTITY »
of Life ...

QUALITY »
of Life is
more important
than
« QUANTITY »
of Life ...
Thank you for your attention.
REFERENCES:

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*Use of comprehensive geriatric assessment in older cancer patients: Recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG)*

Marije E. Hamaker et al.
*The G8 screening tool detects relevant geriatric impairments and predicts survival in elderly patients with a haematological malignancy*
Annals of hematology (Feb 2014, on line)

Pallis A.G. et al
*Questionnaires and instruments for multidimentional assessment of the older cancer patient : what clinicians ned to know*