THE “ELDERLY PROJECT” BY THE FIL (FONDAZIONE ITALIANA LINFOMI):
A TOOL TO DEFINE TREATMENT MODALITY BASED ON THE
PROSPECTIVE MULTIDIMENSIONAL ASSESSMENT OF ELDERLY PATIENTS
WITH DIFFUSE LARGE B-CELL LYMPHOMA

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Background

- DLBCL is the most frequent subtypes of NHL.
- ~60% of DLBCL patients are over age 65.
- ~60% of elderly patients with DLBCL can be cured with standard R-CHOP therapy.
- In real life, many elderly patients with DLBCL are unable to tolerate standard therapy.
- Management of elderly patients with DLBCL in clinical practice is mostly based on physician’s subjective judgment.
- Elderly patients are underrepresented in clinical trials.
Open Questions

What is the best therapy for elderly patients in daily practice?

How to identify treatment goals for elderly patients?
Comprehensive Geriatric Assessment

- Chronological age does not fully explain complexity of elderly patients.

- Comorbidities and functional, social, and biological behaviours are other dimensions of elderly patients.

- Comprehensive Geriatric Assessment (CGA) is a multidimensional tool to define patient’s fitness status: FIT vs NON-FIT

- So far, few studies have assessed CGA in an unselected population of elderly patients with DLBCL.
Comprehensive Geriatric Assessment in FIL Studies

Modified score originally proposed by Balducci (*)

Validation in a small population of elderly DLBCL (**, ***)

“FIL Version” of CGA

ADL  IADL  CIRS-G  Age

(*) Balducci L et al, The Oncologist, 2000
(**) Tucci A et al, Cancer, 2009
(***) Merli F et al, Leuk Lymph, 2013
## Comprehensive Geriatric Assessment in FIL Studies

### Elderly Patients

<table>
<thead>
<tr>
<th></th>
<th>FIT</th>
<th>UNFIT</th>
<th>FRAIL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADL</strong></td>
<td>6</td>
<td>5*</td>
<td>≤ 4*</td>
</tr>
<tr>
<td><strong>IADL</strong></td>
<td>8</td>
<td>7-6*</td>
<td>≤ 5*</td>
</tr>
<tr>
<td><strong>CIRS-G</strong></td>
<td>0 of score 3-4</td>
<td>0 of score 3-4</td>
<td>1 of score 3-4</td>
</tr>
</tbody>
</table>
<pre><code>              | &lt;5 of score 2 | 5-8 of score 2 | &gt; 8 of score 2 |
</code></pre>
<p>| <strong>Age</strong>    | -         | ≥ 80 FIT      | ≥ 80 UNFIT    |</p>

*Residual Functions*
The FIL Experience: Pilot Study

Comprehensive geriatric assessment is an essential tool to support treatment decisions in elderly patients with diffuse large B-cell lymphoma: a prospective multicenter evaluation in 173 patients by the Lymphoma Italian Foundation (FIL)

Tucci A. et al, Leuk Lymph, 2014

- Prospective multicenter observational study
- Purpose: to evaluate the outcome of pts considering both the intensity of treatment received and the results of CGA

- **Inclusion Criteria:**
  - DLBCL
  - Age > 69 years
  - CGA at diagnosis

- Treatment based on physician’s judgment
Overall Survival according to CGA

- median follow up: 24 months
- median age: 77 yrs
  - FIT: 74 yrs
  - UNFIT: 79 yrs
  - FRAIL: 81 yrs
  - FIT vs NON-FIT (84% vs 47%) \( p<0.0001 \)
  - UNFIT vs FRAIL \( p= ns \)

Tucci A. et al, Leuk Lymph, 2014
Overall Survival according to treatment: Curative vs Palliative

**FIT**
- 2-yr OS: 88% vs 25%
- $p<0.0001$

**UNFIT**
- 2-yr OS: 75% vs 45%
- $p=0.32$

**FRAIL**
- 2-yr OS: 44% vs 39%
- $p=0.75$
Conclusions

- CGA is a valid tool to identify elderly DLBCL who can benefit from a curative approach.

- CGA is potentially useful to identify different risk groups among NON-FIT patients.

- A proportion of UNFIT pts may benefit significantly if treated with curative intent (clinical trials should be planned).

- Palliation seems the best choice for frail patients

Tucci A. et al, Leuk Lymph, 2014
ELDERLY PROJECT

“Prospective Collection of Data of Elderly patients (≥ 65 years) with DLBCL undergoing a Multidimensional Geriatric Evaluation at diagnosis

• Aims:
  • To provide clinicians with a standardized tool to assess CGA before treatment start;
  • To validate CGA results on a large series of consecutive patients.
ELDERLY PROJECT

Primary Endpoint
- 2-yr Overall Survival of FIT, UNFIT, and FRAIL patients

Secondary Endpoints
- Type of treatment for each category
- 2-yr Event-free Survival
- 2-yr Progression-free Survival
- Response to therapy

Inclusion Criteria
- Diagnosis of DLBCL
- Age >= 65 years
- CGA at diagnosis
- Informed Consent

Sample Size: 600 patients/3 years
Patient Registration and CGA

FIL WEBSITE (www.filinf.it)
1. General Data
2. Disease Status
3. Activity of Daily Living (ADL)
4. Instrumental Activity of Daily Living (IADL)
5. CIRS-G
Online ADL questionnaire

For each activity report the autonomy degree

5) Continence of feces and urine

- Full control of feces and urine
- Has rare "incidents"
- Needs supervision for controlling feces and urine, uses the catheter, is incontinent

6) Feeding

- Eats without assistance
- Eats with minor assistance at meal times, with help for preparing food as to cut meat or to spread butter on a slice of bread
- Requires assistance to bring the food to the mouth or is fed partly or completely by injection

click to respond
### Online IADL Questionnaire

For each activity report the autonomy degree.

#### 7) Responsibility for own medication:
- Is responsible for taking medication in correct dosages at correct time
- Takes responsibility if medication is prepared in advance in separate dosages
- Is not capable of dispensing own medication
- Not applicable

#### 8) Ability to handle finances:
- Manages day-to-day purchases
- Incapable of handling money
- Not applicable

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**Click to respond**
Online CIRS-G questionnaire

13) Endocrine/Metabolic and Breast disease *:
- No Problem
- Mild
- Moderate
- Severe
- Extremely Severe

14) Psychiatric illness *:
- No Problem
- Mild
- Moderate
- Severe
- Extremely Severe

[Click to respond]
Score and Profile

Select Clinical Study

⇒ FIT protocol
⇒ UNFIT protocol
⇒ FRAIL protocol
Time spent on determining the patient’s status and the therapeutic indications?

< 10 minutes
Elderly Project: Registrations
(30 Sept 2014)

- Italian participating centres: 44
- Study start: Jan. 2014

- Study End: earlier than planned (Jan. 2017)
**Elderly Project: Registrations**  
*(30 Sept 2014)*

<table>
<thead>
<tr>
<th>Category</th>
<th>N. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIT</td>
<td>75 (48%)</td>
</tr>
<tr>
<td>UNFIT</td>
<td>35 (22%)</td>
</tr>
<tr>
<td>FRAIL</td>
<td>48 (30%)</td>
</tr>
<tr>
<td>Total</td>
<td>158</td>
</tr>
</tbody>
</table>

- FIT: 75 (48%)  
- UNFIT: 35 (22%)  
- FRAIL: 48 (30%)  
- Total: 158

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**Diagram:**
- FIT: 48%  
- UNFIT: 22%  
- FRAIL: 30%
Elderly Project: contribution of ADL- IADL – CIRS - Age to Status
(30 Sept 2014)
## Elderly Project: Registrations
*(30 Sept 2014)*

<table>
<thead>
<tr>
<th></th>
<th>FIT N (%)</th>
<th>UNFIT N (%)</th>
<th>FRAIL N (%)</th>
<th>Total N (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong> M</td>
<td>32 (47%)</td>
<td>14 (42%)</td>
<td>23 (52%)</td>
<td>69 (48%)</td>
<td>0.688</td>
</tr>
<tr>
<td><strong>Median Age</strong></td>
<td>73</td>
<td>79</td>
<td>80</td>
<td>76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Stage III-IV</strong></td>
<td>40 (59%)</td>
<td>23 (72%)</td>
<td>31 (70%)</td>
<td>94 (65%)</td>
<td>0.304</td>
</tr>
<tr>
<td><strong>B-Symptoms</strong></td>
<td>15 (22%)</td>
<td>6 (18%)</td>
<td>18 (41%)</td>
<td>39 (27%)</td>
<td>0.039</td>
</tr>
<tr>
<td><strong>IPI 3-5</strong> <em>(interm-high/high)</em></td>
<td>13 (28%)</td>
<td>5 (28%)</td>
<td>14 (47%)</td>
<td>32 (34%)</td>
<td>0.257</td>
</tr>
</tbody>
</table>
## Elderly Project: Planned Therapies

<table>
<thead>
<tr>
<th>Regimen</th>
<th>FIT (n=75) *data available: 48 pts</th>
<th>UNFIT (n=35) *data available: 20 pts</th>
<th>FRAIL (n=48) *data available: 33 pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>None/Palliation</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>RT alone</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>ImmunoCHT</td>
<td>48 *</td>
<td>20*</td>
<td>31</td>
</tr>
<tr>
<td>R-CHOP n.19</td>
<td>R-COMP n.17</td>
<td>R-COMP n.10</td>
<td>R-COMP n.9</td>
</tr>
<tr>
<td>R-DAEPOCH n.2</td>
<td>R-CHOP n.1</td>
<td>R-Myocet n.2</td>
<td>R-BENDA n.4</td>
</tr>
<tr>
<td>R-VNCOPB n.1</td>
<td>R-CVP n.1</td>
<td>R-Chop n.1</td>
<td>R-CVP n.3</td>
</tr>
<tr>
<td>COMP N.1</td>
<td>R-miniCOMP n.1</td>
<td>R-miniCOMP n.3</td>
<td>R-miniCHOP n.3</td>
</tr>
<tr>
<td>Missing n.8</td>
<td>Missing n.1</td>
<td>Missing n.3</td>
<td>Missing n.2</td>
</tr>
</tbody>
</table>

R-CHP n.1
R-CNOP n.1
R-GEMOX n.1
R-EDX n.1
R-COP n.1
R-Cy n.1

### Notes
- FIT (n=75)
- UNFIT (n=35)
- FRAIL (n=48)
- *data available:
  - FIT: 48 pts
  - UNFIT: 20 pts
  - FRAIL: 33 pts
- Regimen:
  - R-CHOP n.19
  - R-COMP n.17
  - R-DAEPOCH n.2
  - R-VNCOPB n.1
  - COMP N.1
  - Missing n.8
Conclusions

CGA:

⇒ objective, reproducible assessment
⇒ used to assist physicians in the initial approach to the patient

ELDERLY PROJECT:

⇒ extend and simplify the use of CGA
⇒ identify new criteria to improve evaluation of elderly patients’ fitness status
⇒ direct the choice of treatment
The FIL Strategy for Elderly Patients
**FIL Elderly Lymphoma Committee:**

1st Line Ongoing Studies and Future Project

**Elderly Project**

- **FIT**
  - ROBUST Study (R-CHOP vs R2-CHOP)

- **UNFIT**
  - GAEL protocol (GA101-miniCHOP)

- **FRAIL**
  - R-Benda Frail
    - COMPLETED

- ReRi protocol
  - (Lenalidomide-Rituximab)
Thanks to:

FIL Elderly Commitee

FIL Centres

All the Patients

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