Treatment of aggressive lymphoma in medically non-fit patients

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Index to detect non-fit patients

Frailty index?
Chemotherapy feasibility index?
Which factors to select patients?

*Based on tools of Geriatricians*

- >70 and one of the following factors
  - > 80
  - ≥3 grade 3 comorbidities
  - *at least one grade 4 comorbidity*
  - dependent in 1+ activity (ADL)
  - *at least one geriatric syndrome*

*Monfardini; Ann Oncol 2005; 16: 1352-8*
Which factors to select patients?

Based on tools of Medical Oncologists

- >70 and one of the following factors
  - *Poor performance status* (WHO 3-4)
  - *Cardiac contra-indic. to doxorubicin*
  - *Low creatinine clearance* (<50 ml/mn)
  - *Neutropenia or thrombocytopenia*
  - *Severe comorbidities*
Which factors to select patients?

**Italian group**
- **Median age**: 83 (70-96)
- **Geriatric features**
  - >80: 73%
  - Dependent: 56%
  - Severe comorb.: 43%
- **aaIPI 2-3**: 56.7%
  - PS 2-4: 60%
  - Stage III-IV: 56.6%
  - Elevated LDH: 46.7%

**EORTC group**
- **Median age**: 78.5 (70-92)
- **Geriatric features**
  - >80: 34.3%
  - Dependent: 53%
  - Severe comorb.: 18.7%
- **aaIPI 2-3**: 72%
  - PS 2-4: 69%
  - Stage III-IV: 50%
  - Elevated LDH: 66%
How many patients?

189 patients

- Incomplete evaluation: 14 patients (7.5%)
- Poor status: 67 patients (35.5%)
- Good status but excluded from phase II: 25 patients (13%)

83 patients (44%)
How to treat frail patients?
Results from phase II trials

Italian cooperative study

- Phase II 2-step design trial (Simon minimax)
- Cautious treatment
  - Vinorelbine 25 mg/m² d1 and d8
  - Oral prednisone 30 mg d1 to d8
  - 6 cycles
- 30 patients included
- Trial stopped after 1st step

Results from phase II trials

Italian cooperative study

- **Prognostic factors**
  - **Median age**: 83 (70-96)
  - **Geriatric features**
    - >80: 73%
    - Dependent: 56%
    - Severe comorb.: 43%
  - **aaIPI 2-3**: 56.7%
    - PS 2-4: 60%
    - Stage III-IV: 56.6%
    - Elevated LDH: 46.7%

- **Toxicity**
  - **Gr 3-4 neutrop.**: 13.3%
  - **Toxic deaths**: 3

- **Efficacy**
  - **ORR**: 40%
  - **CR**: 10%
  - **Med. survival**: 10 m.

Results from phase II trials

EORTC cooperative study

- Phase II 2-step design trial (Briant and Day)
- Cautious treatment
  - Cyclophosphamide 750 mg/m² d1
  - Vincristine 1.4 mg/m² d1
  - Prednisone 40 g/m² mg d1 to d5
  - 6 cycles
- 32 patients included
- Trial stopped after 1st step

P Soubeyran Proc SIOG, Geneva 2005
Results from phase II trials
EORTC cooperative study

Prognostic factors
- Median age 78.5 (70-92)
- Geriatric features
  - >80: 34.3%
  - Dependent: 53%
  - Severe comorb.: 18.7%
- IPI 2-3 72%
  - PS 2-4 69%
  - Stage III-IV 50%
  - Elevated LDH 66%

Toxicity
- Gr 3-4 neutrop. 22%
- Toxic deaths 3

Efficacy
- ORR: 44.5%
- CR: 18.5%
- Med. survival: 10.1 m.
Can we improve over these results?
Next orientations

- Improve treatment efficacy
  - Addition of rituximab
- Decrease risk of toxicity
  - Systematic use of growth factors
  - Tight cooperation with geriatricians
- Better select patients
  - Exclude palliative cases
Next trial: FRAIL06

DLBCL >70
R-CHOP not feasible

Pretreatment work-up
Lymphoma-specific
Geriatric assessment

R-COP
R-COPY

Liposomal doxo reduced dose

Patients managed with geriatricians
With possible interventions

Ancillary studies on biology
What strategy to treat?

Try reduced R-CHOP

Prognostic factors

Geriatric assessment features

Patient’s willing to fight

Palliative ttt
What to conclude?

« Whatever alternatives are adopted, these should no longer be based on enlightened empiricism, but on the results of prospective studies, even if these are small and imperfect. »

Silvio Monfardini

Please include your frail patients in prospective trials!