Elderly patients with CLL

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Objectives

- Achieve an expert recommendation/consensus on appropriate treatment strategy on CLL patients
- Special attention: elderly patients with/without comorbidities
- Develop a manuscript containing a comprehensive official SIOG treatment
- Present recommendations in selected congresses
Aims

- Description of treatment options in CLL and the evidence of their effectiveness and tolerance to define recommendations on CLL
  - Diagnosis
  - Staging
  - Treatment

- Recommendations and propose decisions paradigms for assisting clinicians
Group composition

1. Writing Committee:
   • Multidisciplinary committee consisting of two onco-hematologists, a geriatrician and a specialist in the treatment of side-effects
   • Review of the relevant literature with by a core writing committee
   • Collection of all the material from the taskforce meetings
   • Preparation of a manuscript

2. Review Committee
   • Preparation of the final version of the manuscript
Members of the taskforce

1. Core Writing Committee:
   P. Hillman
   B. Eichhorst
   R. Trappe

2. Extended Writing Committee:
   B. Coiffier
   E. Kimby
   U. Wedding
   A. Ferrajoli

3. Review Committee:
   H. Cohen
   E. Montserrat
   K. Rai
Time lines

1. TC with R. Trappe, P. Hillmen and B. Eichhorst: Outline of manuscript and key literature
2. iwCLL meeting Barcelona (Oct 15–18, 2009): Discussion about the key literature and first developments of the manuscript (R. Trappe, P. Hillmen B. Eichhorst)
3. Writing the first draft manuscript
4. ASH meeting New Orleans (Dec 04–08, 2009): Presentation and discussion of the first draft manuscript
5. Preparation of the second draft manuscript by 02/2010
6. Preparation of the fully styled final draft manuscript by 03/2010
Key areas for discussion:

1. Diagnosis, staging and patient comorbidity assessment

2. Prognostic markers and response predictors in elderly patients

3. Indications for treatment

4. Treatment goal and treatment options
Results

1. Diagnosis, staging and patient comorbidity assessment

   - Diagnosis: blood count, immunophenotype and flow cytometry according to NCI–WG guidelines 2008
     - CLL vs B–cell PLL
     - CLL vs SLL
     - MBL vs CLL

   - Staging:
     - Rai staging system
     - Binet staging system
Results

- Assessment before treatment in general practice:
  - Diagnostic procedures (NCI–WG guidelines 2008)
  - Evaluation of fitness and age by different assessment scores: CIRIS, Charlson
  - Presence of viral infections: CMV, HIV, HBV, HCV
  - Relevance of individual expectations
  - Assessment of disease symptoms
  - Assessment of the response to prior treatment
  - Prediction of the outcome of treatment–associated infections
  - Probability of dose reductions during treatment
Results

2. Evaluation of prognostic factors in elderly patients

- Physically non-fit patients: Response prediction to CLB-based treatment approaches in the context of 17p deletions

- Physically fit patients: Also other markers may impact on treatment decision: subgroup analysis of the CLL–8, CLL–5 and LRF CLL4 trial
Results

3. Indications for treatment
   - According to NCI–WG guidelines 2008

<table>
<thead>
<tr>
<th>Table 2. Recommendations regarding indications for treatment in CLL</th>
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<tr>
<td>Treat with Rai stage 0</td>
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<td>Treat with Binet stage B or Rai stage I or Rai stage II</td>
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<td>Treat with Binet stage C or Rai stage III or Rai stage IV</td>
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<td>Treatment of active/progressive disease</td>
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<td>Treat without active/progressive disease</td>
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General practice is defined as the use of accepted treatment options for a patient with CLL who is not enrolled in a clinical trial. NGI indicates not generally indicated; and RQ, research question.

* Treatment is indicated if the disease is active as defined in section 4.
4. Treatment goal and options

Treatment goal in elderly patients is based on the assessment of comorbidities:

- Control symptoms and/or
- Prolong survival (by achieving a CR)
Treatment intention: CR

1st line:
- MD Anderson data for FCR
- CLL–8 (FC/FCR): Hallek et al., 2009
- CAM307 (Campath/CLB), age: m59 (35–86): Hillmen et al., 2007
- R–Campath, Rai 0/1, 17p–, 30%>70: Zent et al., 2008
Treatment intention: Control of symptoms (1)

1st line:

major trials

- CLL5 (F/CLB), age: 50%>70: Eichhorst et al., 2007
- LRF CLL4 (CLB/F/FC): Catovsky et al., 2007
- 02CLLIII (BEN/CLB), 25%>70: Knauf et al., 2009
- (F/CLB) American Intergroup study: Rai, 2000
- (CLB+R): Hillmen et al., ASH2009
Treatment intention: Control of symptoms (2)

minor trials
- (low dose FC), median age: 71: Forconi et al., 2008
- (FC/FCR) 100%>70: Ferrajoli et al., 2005
- (PCR) 28%>70: Shanafelt et al., 2007

report briefly
- (R+GM–CSF) 100%>70, minimal toxicity: Ferrajoli et al., 2007, Suppl to Leukemia ad Lymphoma 48
- (3R/week +/- eternecept) only mild toxicity, N=36, m60 (30–79): Woyach et al., 2009
Treatment options: relapsed, non-refractory

1. Repeat 1\textsuperscript{st}-line after previous long-lasting remission if acceptable to previous toxicity and current comorbidity

2. Otherwise / alternatives
   - (B): N=17, m67, 5>70: Bergmann et al., 2005
   - (BR): Fischer et al., ASH2008
   - (F): Robertson et al., 1995
   - (F): Shvidel et al., 2003: excessive toxicity in elderly
   - (low dose FC): Fabbri et al., 2004 + Marotta et al., 2000
Treatment options: refractory

- CLL2H (Campath), age: m67 (35–81): Stilgenbauer et al., 2009
- (F–campath), age: m62 (38–80): Elter et al., 2007
- NCRI CLL201 (FCM/FCMR), age: m65 (32–79): Hillmen et al., ASH2007
- (R+HDMP for refractory and 17p– CLL), case series, N=37, age: m67, 22%>78: Bowen et al., 2007
- (R+HDMP for F–refractory), N=14, age: 39–76: Castro et al., 2008
- Ofatumumab: N=138, m64 (41–86): Osterborg et al., ASH2008