"Focus on..." session: lymphoma in the elderly

104 EBV POSITIVE DIFFUSE LARGE B CELL LYMPHOMA OF THE ELDERLY IS AN AGGRESSIVE B CELL NEPLASMA WITH A POST GERMINAL CENTER B CELL PHENOTYPE AND CHARACTERIZED BY NFkB PATHWAY ACTIVATION. EVALUATION OF A WESTERN SERIES OF 47 CASES

S. Montes-Moreno1, L. Odyvist1, J. Diaz Perez1, R. Pajares1, J. Garcia1, M. Mollejo1, C. Ruiz-Marcellan1, M. Adriodos1, N. Ortiz1, R. Franco1, M. Pins1

1Lymphoma Group, Molecular Pathology Department; Spanish National Cancer Center (CNIO), Madrid, Spain

Background: EBV+ DLBCL of the elderly has been recently recognized as a provisional entity by the WHO. Little data in western countries are available. Here we have performed a retrospective clinical, histological and IGH study in a series of 47 EBV+ DLBCL in elderly patients (mean age 69 years (48-91)) retrieved from the consultation files of the CNIO in a period of 6 years.

Material and methods: HE, IHC and ISH for EBV (EBER) were performed using conventional protocols and antibodies. Cases were classified according to the Cell of Origin-Grouping by D Ludwig (2010) using CD5 and Hans algorithms. Relevant clinical information was retrieved from referral centers.

Results: The series includes 31 male and 16 female. Most cases present at nodal locations (68%) while extranodal cases (32%) appeared in soft tissue, spleen, tonsil and gastrointestinal tract, among others. Morphologically most of the cases here studied showed a pseudohodgkin-like B cell population (46 cases) with areas of geographic necrosis (14 cases). All cases were CD20+ and commonly co-expressed CD30 (41/46) and very rarely CD15 (4/42). EBER was always positive and only 4 cases were negative for EBV-LMP1. Most cases belong to the NON-GC/ABC category by Hans (39 NON GC vs 2 GCB, 7 NY) and conventional protocols and antibodies. Cases were classified according to the Cell of Origin-Grouping by D Ludwig (2010) using CD5 and Hans algorithms. Relevant clinical information was retrieved from referral centers.

Conclusions: Our results demonstrate that EBV+ DLBCL of the elderly is aggressive and has a post GC B cell phenotype. This differentiation state is related with prominent classical and alternative NFkB activation which in turn is partially driven by EBV.

105 COMPREHENSIVE GERIATRIC ASSESSMENT-ADAPTED CHEMOTHERAPY IN ELDERLY PATIENTS (> 70 YEARS) WITH DIFFUSE LARGE B-CELL NON-HODGKIN'S LYMPHOMA (DLBCL): FINAL RESULTS AND LONG TERM FOLLOW-UP

U. Tirelli1, L. Fratino1, M. Balzarotti2, L. Uziel3, A. Giacalone1, A. Ferreri4, A. Santoro2, M. Mollejo1, C. Ruiz-Marcellan1, M. Adrados1, N. Ortiz1, R. Franco1, M. Pins1

1Medical Oncology A, National Cancer Institute, Aviano, Italy, 2Medical Oncology and Hematology, Humanitas Institute, Rozzano, Italy, 3Hematology, San Paolo Hospital, Milan, Italy, 4Oncology, San Raffaele Hospital, Milan, Italy

Background: R-CHOP is the standard treatment for elderly patients (pts) with DLBCL. Many pts aged 70 years (yrs) or more are unable to receive R-CHOP and the majority of them are excluded from clinical trials. Comprehensive geriatric assessment (CGA) is a useful instrument to predict the clinical outcome of elderly pts with cancer. Within the GOL (Gruppo Oncologico Linfomi) we started a phase II study aiming to evaluate feasibility and activity of a CGA-driven chemotherapy for elderly pts with DLBCL.

Material and Methods: Pts with no comorbidity received CHOP/R-CHOP; pts with mild cardiopathy received epirubicin instead of doxorubicin; in pts with moderate/severe cardiopathy the use of anthracyclines was omitted; pts with diabetes did not receive prednisone, pt with previous pneumonitis. CHOP was decided according to CGA; pts with a good score received 6 cycles of CHOP; pts with poor score (ADL<5 or IADL<5) received only 4 cycles. The dose-intensity for CHOP was 85% of the dose-intensity of R-CHOP. Median age was 73 yrs and stage III-IV were diagnosed in 25% of pts. Sixty-one percent of pts received full doses of CT; 25% received 75% of dose and 10% received 50% of dose.

Results: One hundred and sixty pts (41 males and 59 females) have been treated. The median age was 75 yrs and stages III-IV were diagnosed in 51% of pts. Sixty-one percent of pts received full doses of CT; 25% received 75% of dose and 10% received 50% of dose. Survival rates for elderly patients (pts) (60 years) with HL are disproportionately inferior to those achieved by younger pts. Historically, 5-year survival was approximately 60% for young pts and 40% for elderly pts. Since 1995, new chemotherapy regimens have been developed for HL. Many of these regimens are more intensive than CHOP. A majority of these new regimens include high-dose chemotherapy and autologous stem cell transplantation (ASCT) as consolidation therapy. One of these new regimens that have been used extensively is R-CHOP14. R-CHOP14 compared to R-CHOP21 in elderly patients with diffuse large B-cell lymphoma (DLBCL): results of the second interim analysis of the LH3N03-6B GELA study of the second interim analysis of the randomized phase III trial LH3N03-6B, comparing both regimens, was given according to physician decision. Primary objective was to evaluate the efficacy of R-CHOP14 compared to R-CHOP21 as measured by the EFS.

Results: 602 pts were randomized, 600 were evaluable, 304 with R-CHOP14 and 296 with R-CHOP21. Median age was 70 years. Pts characteristics were similar in both arms. Percentage of pts with baseline IPI=3-5 was 72% in R-CHOP14 arm and 78% in R-CHOP21 arm. Median interval between 2 cycles was 14 d in R-CHOP14 arm and 21 d in R-CHOP21 arm. In R-CHOP14 arms, 89% of cycles were administered with G-CSF. Median dose-intensity for R-CHOP14 arm was 88% for cyclophosphamide and doxorubicin. There was no difference in median dose-intensity according to G-CSF administration at first cycle. Response rate (CR+CRu) was 72% in R-CHOP14 arm and 75% in R-CHOP21 arm (p=0.42). The 3-y EFS was 57% in R-CHOP14 arm and 60% in R-CHOP21 (HR 1.03; CI95% 0.81-1.31; p=0.81). Similar trend was observed for 3-y PFS (60% vs 62%; HR 0.98; CI95% 0.77-1.26; p=0.89) and 3-y OS (70% vs 72%; HR 0.98; CI95% 0.74-1.30; p=0.99).

There was no PFS difference according to dose-intensity. Grade 3-4 toxicities were similar in both arms with the exception of neutrophils and hemoglobin toxicities, more frequent in R-CHOP14 arm leading to higher rate of red cell transfusions (43% vs 32%). In contrast, platelet toxicity was more common in R-CHOP21 arm. Median number of nights of hospitalization was 9 in R-CHOP14 arm and 7 in R-CHOP21 arm.

Conclusion: Results of this second interim analysis did not support the hypothesis of higher efficacy of dose dense R-CHOP14 over R-CHOP21.

107 EFFICACY AND TOLERABILITY OF ABVD AND STANFORD V FOR ELDERLY ADVANCED-STAGE HODGKIN LYMPHOMA (HL): ANALYSIS FROM THE PHASE III RANDOMIZED US INTERGROUP TRIAL E2496


1Hematology/Oncology, University of Massachusetts, Worcester, United States, 2ECOG Statistical Center, Harvard University, Boston, United States, 3Hematology/Oncology, Northwestern University, Chicago, United States, 4James P Wilmot Cancer Center, University of Rochester, Rochester, United States, 5Oncology, Washington University, St. Louis, United States, 6Centre for Lymphoma Cancer, BC Cancer Agency, Vancouver, Canada, 7Radiation Oncology, Penn State Cancer Institute, Hershey, United States, 8Radiation Oncology, Princess Margaret Hospital, Toronto, Canada, 9Hematology/Oncology, Georgetown University Hospital, Washington DC, United States, 10Medical Oncology, Stanford University, Stanford, United States, 11Hematology/Oncology, University of Wisconsin, Madison, United States, 12Radiation Oncology, Stanford University, Stanford, United States, 13Clinical Development, Genetech, Inc., San Francisco, United States

Background: Survival rates for elderly patients (pts) (60 years) with HL are proportionately inferior to those achieved by younger pts. Historically, 5-year specific survival was 72%.

Conclusion: Our results demonstrate that a CGA-driven approach is feasible in elderly pts with DLBCL. This strategy allows offering a curative approach to all pts with aggressive NHL, avoiding to under treat pts with a potentially cured disease or over treat pts with severe comorbidities.
Table 1. Survival comparisons.

<table>
<thead>
<tr>
<th>Survival</th>
<th>Elderly (≥ 60 years)</th>
<th>Non-Elderly (&lt; 60 years)</th>
<th>Log rank p</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-year FFS</td>
<td>55/43</td>
<td>76/769</td>
<td>0.0014</td>
</tr>
<tr>
<td>5-year FFS</td>
<td>46/43</td>
<td>74/769</td>
<td></td>
</tr>
<tr>
<td>3-year OS</td>
<td>69/43</td>
<td>93/769</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5-year OS</td>
<td>56/43</td>
<td>90/769</td>
<td></td>
</tr>
</tbody>
</table>

**Methods:** We analyzed the outcomes and tolerability for pts ≥ age 60 years with advanced-stage HL treated in E2496. Pts were randomized to receive chemotherapy (CT) with ABVD x 6–8 cycles with radiotherapy (RT) for bulky mediastinal disease or the Stanford V regimen (12 weeks of CT and RT 36 Gy to sites > 5 cm). The primary endpoint was FFS, defined as time to either progression/relapse or death. The t-test or Fisher’s exact test was used to compare pt characteristics and response rates; the stratified log-rank test was used for FFS and overall survival (OS).

**Results:** Of 812 eligible pts enrolled, 43 were ≥ 60 years of age (n=23 ABVD and n=20 Stanford V). Pt characteristics between CT arms were balanced; data for the 43 elderly pts included: median age 65 (60-83 years); stage: II 7%, III 69%, IV 23%; R symptoms 47%; and IPS 4 16%. Several differences were noted comparing pts ≥ 60 vs < 60 years: mixed cellularity cell type (35% vs 13%, respectively, p=0.0004, OR=3.52) and ECOG PS 0 (35% vs 58%, respectively, p=0.004, OR=0.38). CT dose modifications, as required by protocol, were common with 84% of all elderly pts having at least 1 dose reduction. CT was tolerated relatively well; besides neutropenia, there were 11 total grade 4 toxicities (dyspnea n=3, motor and sensory neuropathy n=2 each, hypoxia n=1, constipation n=1, infection n=1, myalgia n=1). The treatment-related mortality rate was 5% (n=1 pulmonary with ABVD and n=1 infection with Stanford V). Among all elderly pts, overall response rate (ORR), complete response (CR), FFS, and OS did not differ between CT arms. Therefore, treatment arms were pooled and stratified for an exploratory analysis comparing pts ≥ 60 vs <60 years. The ORR (70% vs 78%, respectively, p=0.19) and CR rates (65% vs 71%, respectively, p=0.49) did not differ for elderly pts compared with non-elderly pts; however, 3- and 5-year FFS and OS were significantly inferior for elderly pts (Table 1).

**Conclusions:** ABVD and Stanford V had comparable efficacy and tolerability among elderly advanced-stage HL pts. When comparing pts ≥ 60 years vs <60 years, pts in the contemporary era this trial was conducted, we observed similar ORR and CR rates, but inferior FFS and OS. These observations suggest a potential difference in disease biology, underscoring the continued need for novel therapeutic approaches for elderly HL.

**Methods:** We analyzed the outcomes and tolerability for pts ≥ age 60 years with advanced-stage elderly HL in the modern era.

**Methods:** We analyzed the outcomes and tolerability for pts ≥ age 60 years with advanced-stage elderly HL in the modern era.

**Conclusions:** Autologous stem cell transplantation is feasible and of potential benefit in selected elderly patients with lymphoma. Age alone need not exclude patients with good functional status and limited comorbidity.