**450 CONSOLIDATING RADIOThERAPY IN HIGH-RISK NON-HODGKIN’S LYMPHOMA: STILL AN APPEALING CONCEPT!**

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Introduction: The primary treatment for stage II aggressive non-Hodgkin’s lymphoma (NHL) consists of 6 to 8 cycles of chemotherapy. The role of consolidating radiotherapy for high-risk patients is uncertain. Therefore, we retrospectively analysed the outcome of all our patients consecutively treated with curative intent with consolidating radiotherapy after chemotherapy.

Methods: We treated 181 patients from 1972 to 2005 for stage II NHL. The vast majority (160 patients) was irradiated as part of initial combined modality treatment. Of those patients, 76 had a complete response and 84 had residual disease after chemotherapy. Another 21 patients were irradiated after salvage chemotherapy for recurrent disease. All patient files were reviewed and updated if necessary.

Results: Median age at the time of radiotherapy was 61 years (range 9 – 85); 105 were male and 76 female. The median follow-up time for surviving patients is 4.7 years (0.3-33). Radiotherapy was given according to the “iceberg principle” and to the “involved field” extended field and “involved nodal” concept or to residual disease. In 49 (22%), 100 (55%), 4 (2%), 18 (10%) and 6 (6%) patients, respectively. The 5-year overall survival is 63% in the initially irradiated group with a CR after chemotherapy, 58% in CR initially (168 patient group with residual disease) and 35% in patients who irradiated for a recurrence. Disease free survival at 5 years is 61%, 60% and 37%, respectively. In 28 of the 73 patients who developed a recurrence, the disease recurrence was at least partially within the original radiation field. The acute radiotherapy related toxicity was grade 1 or less in 145 patients (80%), grade 2 in 34 (19%) and grade 3 in 2 patients. Late toxicity was not reported.

Conclusions: The outcome of our patients in this non-selected group of high-risk NHL treated with consolidating radiotherapy after chemotherapy compares favourably with the results as published in the literature. Radiotherapy-related toxicity was very mild. The presence of residual disease after chemotherapy and the radiotherapy technique had no influence on the outcome but patients who were treated for recurrent disease experienced a worse prognosis.

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**451 THE EFFECT OF DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) TREATMENT REGIMENS ON SURVIVAL: A PROSPECTIVE COHORT STUDY**

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Background: Most data on treatment and outcome of DLBCL patients (pts) come from clinical trials on selected groups of pts. However, data on large unselected cohorts is still unavailable.

Material and Methods: DLBCL pts prospectively registered in SNLG between 1990 and 2003 were evaluated. Further inclusion criteria were: age at diagnosis ≥18 years and primary nodal origin of disease; pts treated with Rituximab were excluded.

Results: 1863 pts were included (median age 66 years (y), range 18-98y); 711 pts were 50-69 and 1152 >60y; 49% pts were male. Anthracycline based chemotherapy (CT) was the most frequently used treatment (75%), followed by radiotherapy (RT) alone (7%), other CT (6%) and autologous stem cell transplantation (ASCT) in 1st remission (5%); 7% of patients received no CT or RT. Among pts 50-69y there were statistically significant more males, pts with lower ECOG and IPI, and pts with RT only (41%) and lowest in pts with ASCT (6%), followed by pts treated with anthracycline based CT (46%) and pts with RT only (41%) and lowest in pts with other CT (14%) and in pts with ASCT (10%). p<0.05. 5y OS and SFS were higher in pts 50-69y and in pts with ASCT and II, p<0.05. Using the IPI 4 different groups were distinguished with 5y PFS and OS of 55%.

Conclusions: The outcome of unselected DLBCL pts in the pre-Rituximab era was unsatisfactory, especially in high-risk and elderly pts. Prognostic value of IPI was limited in high-risk groups. The question of whether the addition of Rituximab to standard therapy has improved the outcome in all or in only some group of pts needs to be evaluated in unselected cohorts of pts.

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**452 FACTORS INFLUENCING TIME TO INITIATION OF CHEMOTHERAPY IN ELDERLY PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL)**

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Background: DLBCL is an aggressive lymphoma for which treatment should be initiated quickly. The purpose of this study is to identify factors associated with the initiation of chemotherapy and the incremental cost of care.

Methods: We analyzed DLBCL patients diagnosed from 1998 to 2002 with 1 year of non-HMO coverage prior to diagnosis in the SEER-Medicare dataset. Time to initial cheomotherapy initiation (CT) and costs of care were identified through claims for inpatient, outpatient and physician services through 2005. Costs were compared to a random sample of non-cancer Medicare patients using linear regression. Time to CT was assessed using proportional hazards regression with censoring for death and end of coverage. Models were adjusted for age, race, gender, comorbidity score, year of diagnosis, region (cost model) and stage (time model). CT was classified using all outpatient claims after diagnosis.

Results: There were 903 patients included. The mean age at diagnosis was 77 years, 86% were white, 33% were stage IV and 53% were alive 12 months after diagnosis. The mean monthly cost for the first year after diagnosis was $8,003 higher in DLBCL patients than in typical Medicare patients. Only 71% of patients received CT within the follow up period. Median time to first CT was 57 days. The most common initial CT used was CHOP+R (63%). Older age and greater comorbidity burden were associated with longer times to first CT (p<0.01). Black and other race were also associated with a significantly longer time to first CT (p<0.01).

Conclusions: DLBCL is associated with an increased incremental cost of care. The time to CT initiation was associated with several patient characteristics including age and race.

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**453 ULTIMATE OUTCOMES OF PATIENTS WITH RECURRENT DIFFUSE LARGE B CELL LYMPHOMA WHO DO NOT RESPOND TO SECOND-LINE CHEMOTHERAPY**

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Background: Patients with diffuse large B cell lymphoma (DLBCL) who relapse after or are refractory to initial therapy can in some cases experience long term disease free survival after second-line chemotherapy alone or followed by autologous stem cell transplantation. The major predictor of outcome for patients undergoing autologous transplant is response to prior (second-line) chemotherapy. Patients not responding to second-line regimens may receive third-line or subsequent chemotherapy regimens in hopes of achieving response and proceeding to transplant, but available outcome data from this group are limited.

Methods: We used pathology and treatment records to identify patients with recurrent DLBCL (excluding transformed lymphoma) at Weill Cornell Medical Center for whom data on response to second-line chemotherapy could be determined. An online social security database verified survival. Median overall survival (OS) was calculated by the Kaplan-Meier method.

Results: Sixty patients with relapsed or refractory DLBCL who underwent second line chemotherapy were identified. Chemotherapy consisted of ifosfamide-containing regimens in 54 patients (90%), platinum-containing regimens in 49 (82%) and included rituximab in 25 (42%). Thirty-nine patients (69%) achieved at least partial response (R), while 21 patients (35%) did not respond (NR). Median OS was 4 months (range 1-74) in the NR group, and 57 months (range 3-108) in the R group. Only 4 patients in the NR group (19%) survived for greater than one year. Of 19 NR patients who underwent third-line therapy, only 2 of 13 with available response data achieved a clinical response and underwent autologous transplantation. One patient remained in remission for 3 months, with OS 7 months, while the other patient is alive in remission 72 months after transplant.

Conclusion: Patients with recurrent DLBCL who do not respond to second-line chemotherapy have poor outcomes, with only rare patients achieving extended survival following subsequent chemotherapy. Clinical trials of novel therapeutic regimens should be prioritized as management strategies for these patients.
**456 EXPRESSION OF CD43 IS AN IMPORTANT NEGATIVE PROGNOSTIC MARKER IN DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL)**

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**Abstract:**

CD43 is a membrane protein expressed on all leukocytes except resting B-cells, this does not seem to be the whole explanation of its significant prognostic impact. While it is possible that explanations for the adverse effect of CD43 in lymphomas. There are no clear biological mechanisms involved extranodal sites (p=0.031). The prognostic impact of CD43 expression was of the same order of magnitude as that of IPI.

**Results:** Fifty-two pts (median age: 68 yrs: 29M/23F). All cases received chemotherapy based in CHOP regimen. Cases were subclassified using CD10, BCL-6 and MUM1. The statistical method was descriptive and survival was calculated using the Kaplan-Meier method.

**Conclusion:** Immunohistochemical expression of CD10, BCL-6 and MUM1 are able to determine the GCB and non-GCB subtypes of nodal DLBCL and predict survival.

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**459 P57KIP2 GENE METHYLATION IS USEFUL TO DETECT MINIMAL RESIDUAL DISEASE IN DIFFUSE LARGE B CELL LYMPHOMA**

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In diffuse large B cell lymphoma (DLBCL), the universal method for evaluation of minimal residual disease (MRD) in bone marrow has not been established. The BCL2/IgH gene rearrangement is usually used to detect and quantify MRD in follicular lymphoma (FL), but the frequency of this rearrangement is relatively low in DLBCL. We revealed that the promoter region of p57KIP2 gene is frequently methylated in DLBCL.

**Methods:** We analyzed lymphoid cell line DNA, tumor DNA from 64 patients with DLBCL and 4 patients with FL, and 11 peripheral blood mononuclear cells (PBMCs) from healthy volunteer. The bisulfite-modified DNA was used as a template for real-time quantitative methylation-specific PCR (Q-MSP).

**Results:** In clinical samples (tumor DNA), p57KIP2 gene methylation was detected by Q-MSP in 72% (46/64) DLBCL, 50% (2/4) FL, 0% (11/11) in normal PBMCs. Using cell line DNA, which was fully methylated in promoter region of p57KIP2 gene, we determined the detection limit of Q-MSP assay. The methylated DNA could be detected in the presence of a 10,000-fold excess of unmethylated DNA by Q-MSP. In calculation, it meant the possibility to detect 6.6-8.0 genome per one reaction.

**Conclusion:** The sensitivity to detect MRD by this method was found to be equivalent to quantitative PCR for BCL2/IgH major breakpoint region. This method is thought to be conventional and widely applicable to the detection of MRD in DLBCL.
Introduction: The importance of p63 protein for diffuse large B-cell lymphoma (DLBCL) is still unclear from the pathological and clinical perspective. In order better understand this protein and improve the prognostic evaluation of DLBCL patients with high intermediate to high age-adjusted International Prognostic Index (aIPI) risk, the impact of p63 expression on achieving complete remission (CR), disease-free survival (DFS) and overall survival (OS) was studied in correlation with markers associated to the cell origin in the germinal center (GC) or out of germinal center (NGC).

Material and methods: Seventy-three patients aged under 60 years old were examined by immunohistochemistry using a monoclonal antibody p63 clone 4A4 clone. Results: The authors found that subset of DLBCL 37 (50.7%) were positive when we considered them as both GC and NGC, and 11 (15.1%) when the threshold was 50% of neoplastic cell. When only patients showing more or equal cells of were considered positive, there were statistically significance for DFS (p=0.016) for patients with more than 50% of positive cells than cases with less than 50% positive cells to p63.

Conclusion: Despite their controversy, our results showed that p63 expression can be used in the risk stratification of DLBCL patients with high intermediate to high aIPI risk.

640 REDUCED DOSE OF NON-PEGYLATED LIPOSOMAL DOXORUBICIN WITH CYCLOPHOSPHAMIDE, VINCristINE AND Prednisone ≠ RITUXIMAB FOR previously untreated ELDERLY PATIENTS WITH AGGRESSIVE LYMPHOMA NON-SUITABLES FOR STANDARD CHEMOTHERAPY

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Background: CHOPE contains a higher dose of doxorubicin (D) and cyclophosphamide (C) and acts better than CHOP. A lower dose of D, C and without prednisone (P) has been proposed for the elderly and lymphoma control with a published 5 year EFS of 40.2%/69.4% (32-48/62-77%) in the elderly/younger pts and a 5 year OS of 49.8%/85.1% (41-58/79-90%) in the NHL 2821 trial for CHOEP-14, inferior esp. for the younger pts. The Id dose increase does not translate into higher efficacy but increases hematotoxicity. Therefore Doxorubicin remains the standard anthracycline for the treatment of aggressive NHL.

462 IN DIFFUSE LARGE B CELL LYMPHOMA PATIENTS R-CHOP14 SEEMS TO OVERCOME THE NEGATIVE PROGNOSTIC SIGNIFICANCE OF B CELL ORIGIN

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Approximately half of all patients with diffuse large B cell lymphoma will be cured of their disease by primary therapy the remaining die of the disease. Gene-expression profiling identified two major subgroups: germinal centre B (GCB) cell or non-germinal centre (non-GCB). In some recent papers the GCB group showed a significantly better survival than non-GCB group. Immunohistochemistry (IHC) has been evaluated as a surrogate for this molecular classification. The aim of this study was to define retrospectively the B-cell origin of 35 patients (pts) treated with R-CHOP14 and to evaluate if the dose-dense immune-chemotherapy could improve their clinical outcome. We performed IHC stains on formalin-fixed paraffin-embedded tissues from diagnostic biopsies and based on the algorithm published by Hans et al. we subdivided the pts in GCB origin and non-GCB origin. Twenty-four pts were male, 18 were stage III-IV, 17 showed bulky disease. Eighteen pts showed abnormal LDH value, the IPI was intermediate-high risk 9 in 9 and high risk in 4 pts. According to IHC analysis 15 pts derived from germinal centre and 20 from non-germinal centre, 17 pts presented a positive bcl2. Twenty-five pts (71%) obtained a CR, 7 a PR and 3 were NR. All pts with PR and 2 out 3 NR derived from germinal centre. Four out 25 CR pts experienced relapse, three (75%) derived from non-germinal centre. Eight pts died five derived from non-GCB. After a median period of observation of 13 months (range 3-65 months) the overall survival (OS) was 71% and the failure free survival (FFS) was 57%. The statistical analysis was performed comparing the B cell origin and clinical characteristics.

In univariate analysis normal Beta2 microglobulin and ESR, low-intermediate risk IPI was significantly higher in low and low-intermediate IPI risk patients it was the only factor that influenced the FFS. In conclusion even if few patients were evaluated we can point out that the intensification could improve the OS in patients with non-GCB lymphoma. Further analysis with larger sample sizes of DLBCL pts are needed to verify this preliminary observations.

463 FCGR3A POLYMORPHISMS NOT RELATED TO CLINICAL OUTCOME AFTER INITIAL R-CHOP THERAPY IN PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA

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Introduction: The addition of rituximab to CHOP chemotherapy (R-CHOP) improved survival of patients with diffuse large B-cell lymphoma (DLBCL). Antibody-dependent cellular cytotoxicity (ADCC) is thought to be a predominant mechanism of rituximab activity in clearance of lymphoma cells. FCGR3A is mainly mediated by Fc gamma receptor (FCGR) and several studies suggested that FCGR polymorphism can influence antitumor efficacy of rituximab. The aim of this study was to determine the possible impact of FCGR3A polymorphism on the outcome in 31 patients with DLBCL initially treated with R-CHOP.

Methods: Polymorphism within FCGR3A locus, including FF, VF, and VV alleles was determined by allele-specific PCR. End points were overall response rate (ORR), including complete (CR) and partial remissions (PR), progression free (PFS) and overall survival (OS).

Results: The distribution of FCGR polymorphic alleles was 35% of FF, 52% VF, and 13% VF. ORR were 90.4% in FF, 93.7% VF, and 100% in VF carriers, including 54.5%...
6.87%, 30% CR and 36.3%, 25%, 50% PR, respectively. Treatment responses, PFS, and OS didn’t differ significantly between studied groups.

Conclusions: These data indicated that initial response to R-CHOP in the studied group of DLBCL patients was not related to FCGR3A polymorphism.

464 EFFICACY OF CONVENTIONAL SECOND-LINE SALVAGE THERAPY IN PATIENTS WHO HAVE PROGRESSIVE DISEASE AFTER FIRST-LINE SALVAGE THERAPY WITH RELAPSED OR REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA

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Introduction: ICE, DHAP and ESHAP are considered conventional platinum-containing salvage therapy for relapsed or refractory diffuse large B-cell lymphoma. The optimal treatment for progression after 1st line salvage therapy is not standardized.

Methods: We retrospectively analyzed the efficacy of conventional platinum-containing salvage regimen as 2nd line salvage therapy for diffuse large B-cell lymphoma.

Results: The outcome of 28 patients (M:F=13:7) (median age=62, 28-76) with diffuse large B-cell lymphoma, who have previously received conventional salvage therapy, was analyzed. Sixteen of the patients were treated adding rituximab to conventional salvage therapy. In all 20 patients, responses were six with complete remission (CR) and two with partial response (PR), resulting in 62% overall response (ORR). With median follow-up of 10 months, estimated 1yr progression free survival (PFS) was 31% and 1yr overall survival (OS) was 55.7%. Four patients who were potential candidates for autologous stem cell transplantation (ASCT) were able to receive ASCT. Seven patients (57.1%) achieved CR. 2 confirmed at 6 weeks and one each at 3 months and 6 months.

Conclusions: Treatment with 131I-rituximab may potentially provide effective and safe chemoimmunotherapy with 131I-rituximab with an additional treatment imminent prior to planned interim post treatment.

465 RADIOIMMUNOTHERAPY WITH 131I-RITUXIMAB FOR RELAPSED DIFFUSE LARGE B CELL LYMPHOMA: A PHASE II STUDY PRELIMINARY REPORT

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Aims: Radioimmunotherapy (RT) with 131I-rituximab is effective treatment of relapsed and refractory indolent non-Hodgkin Lymphoma with an overall response rate (ORR) of 78% and complete remission (CR) in 53%. The role of RT in relapsed Diffuse Large B Cell Lymphoma (DLBCL) is less clear. Our single institution phase II study to treat 40 patients was designed to assess the efficacy and safety of 131I-rituximab in patients unsuitable for aggressive chemotherapy and/or BMT.

Methods: Patients with relapsed or refractory DLBCL received induction with 4 once weekly 375 mg/m2 rituximab doses and a single individualized 131I-rituximab therapy activity precipitated upon 0.75 Gy/hole body radiation absorbed dose on an outpatient basis. Lugols iodine was administered to prevent thyroid irradiation. Consolidation therapy commenced day 56 and continued bi-monthly with unlabelled rituximab 375 mg/m2 for 6 treatments. Patients were monitored with weekly blood counts until recovery from nadir. Follow up PET/CT scans were performed at 6, 12, 24 and 52 weeks post treatment.

Results: Twelve patients have been enrolled. Nine patients have received treatment with 131I-rituximab with an additional treatment imminent prior to planned interim safety analysis. Eight patients are evaluable for response. Two patients had a severe deterioration in performance status following enrolment and were not treated. Four patients achieved CR, 2 confirmed at 6 weeks and one at each 3 months and 6 months with PFS of 26, 21, 8 and 5 months. One patient had stable disease at 6 weeks. Three patients with PD had median IPI score of 3 and raised LDH compared with the responder’s median IPI 2 and normal LDH. Grade 4 neutropenia occurred in one patient. There was no grade 4 thrombocytopenia. All 9 treated patients had had rituximab therapy.

Conclusions: Treatment with 131I-rituximab may potentially provide effective and safe therapy in some patients with relapsed DLBCL who may be elderly or otherwise not suitable for intensive chemotherapy or BMT. Patients with refractory and/or rapidly progressive and bulky disease are least likely to respond to radioimmunotherapy.
**471 R-CHOP VS R-EPOCH IN DIFFUSE LARGE B-CELL LYMPHOMA CS IIBULKY-IV. THE SERBIAN STUDY LYMPHOMA GROUP (SLG) EXPERIENCE**

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**Purpose:** High-dose polychemotherapy with autologous bone marrow transplantation is standard treatment for relapse and refractory lymphoma. Due to age, poor performance status and presence of comorbid diseases significant number of patients is not eligible for this modality of treatment. In this prospective cohort we evaluated the efficacy, toxicity, and feasibility of modified salvage chemotherapy regimen in a single center setting.

**Patients and Methods:** We tested a modified salvage regimen protocol IMPV16 containing dolsamide (given at dose 1000 mg/m² from day 1 to day 3) with mesna support and etoposide (given at dose 100 mg/m² from day 1 to day 2), without metotrexate in patients with relapse and refractory intermediate- and high-grade Non-Hodgkin’s lymphoma. Chemotherapy was repeated every third week, three to six times according to response. Fifteen patients entered the trial. The median age was 61 years. All 15 patients had stage III or IV disease. The distribution among international risk categories-low, intermediate-low, intermediate-high, and high was 6.7%, 60%, 20%, and 12.3%, respectively.

**Results:** Of 14 eligible patients, two (13.3%) had a complete remission and four (28.6%) a partial remission, eight patients had progressive disease (53.3%). One patient was lost for follow up. Median time to progression was 18.5 months. After a median follow-up time of 12.5 months, the estimated time to relapse was 63%.

**Conclusion:** Our preliminary data suggests that VP-IFO regimen is relatively efficient, safe and feasible for treatment of patients with relapse and refractory aggressive Non-Hodgkin’s lymphoma, which are not candidates for high-dose polychemotherapy with autologous bone marrow transplantation. Further study is needed in order to confirm our results.

**472 RITUXIMAB RETHERAPY IN AGGRESSIVE NON HODGKIN LYMPHOMA AFTER INITIAL IMMUNOCHEMOTHERAPEUTIC TREATMENT WITH RITUXIMAB**

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The efficacy of chemotherapy combined with rituximab in patients with relapsed or progressive Non Hodgkin lymphoma (NHL) after initial treatment with rituximab containing chemotherapy was evaluated. Of 17 eligible patients, ten had diffuse large B-cell lymphoma with one having Richter’s syndrome. Seven had mantle cell lymphomas. In 64% of the patients the IPI was ≥2. The median age was 53 years (36-72 years) at the time of diagnosis. 12 patients were male. Objective response to first immunochemotherapy (ICT) was seen in 12 (70.5%) patients and included complete remission in six of them. All patients with NHL had objective response. After relapse, 58% (7/12) responded again to ICT: two had a CR and five a PR. Non responder to first line ICT did not respond to second ICT (3/5). Eight patients did not receive high-dose chemotherapy. Four responded to second ICT (3CR/PR). But within less than...
12 months, 3 of these patients died due to NHL, two are alive but in progression at 12 and 34 months, one patient was lost to follow up in PR 10 months after second ICT. Nine patients received high dose chemotherapy with stem cell transplantation (SCT). Four patients received autologous or syngenic SCT, respectively. One patient with MCL is in remission 43 months after radioimmunotherapy. One patient after autologous SCT is in PD 21 months after start of second ICT, respectively 6 months after SCT. Two received a second – that time autologous SCT due to residual disease. CR was achieved out of 7 patients after autologous SCT with no signs of progression in the seventh patients. One relapse was seen in the observation time up to 11 months. But success is hampered by high mortality. Due to infections four patients died 3, 6, 9 and 26 months after autologous SCT without signs of NHL. At 35 and 31 months post autologous SCT only 2 patients are alive and in CR. In relapsed aggressive NHL second response to ICT with rituximab is seen in 58% of the patients. But the risk of further relapses is high. In these patients high-dose radioimmunotherapy and autologous SCT are options to induce long term remission or maybe cure.

473 3 YEARS OUTCOME OF NEUALLY DIAGNOSED DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) PATIENTS TREATED WITH IMMUNOCHEMOTHERAPY – SERBIAN LYMPHOMA STUDY GROUP (SLG) EXPERIENCE

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Background: DLBCL is the most common type of Non Hodgkin lymphoma. Recent international randomized studies confirmed the benefit of overall response rate (ORR) and overall survival (OS) in patients (pts) treated with anti CD20 monoclonal antibody-immunochemotherapy showed significant improvement of the outcome of newly diagnosed DLBCL pts. CS, bulky disease and PS haven’t the predictive value on the outcome, so new parameters need to be tested for predictive scoring system.

Methods: During the last 7 yrs, 113 pts with newly diagnosed DLBCL were treated with R-CHOP/CHOP-like regimens. On presentation the International Prognostic Index (IPI) and bulky disease were determined. The median follow up was 36 months (range 1–84 months).

Results: The mean age was 52.4±14.3 yrs, range 22–92(69% of pts were <60 yrs). Gender distribution was 65 male/50 female. 7 pts (6.19%) were in I CS, 41(36.28%) in II CS, 25(22.12%) in III CS and 40 (35.40%) in IV CS. The IPI distribution was as follows: low risk 39 pts (34.53%), intermediate risk 67 pts (59.29%) and high risk 7 pts (6.19%). Bulky disease had 36 pts (31.86%). 70 pts (63.95%) had ECOG performance status (PS) 0, 23 pts (20.95%) had PS1 and 20 pts (17.7%) had PS 2. The ORR (CR+PR) was 76.99%. CR was better in pts <60 yrs (border line significance, p=0.056) and in low/low intermediate IPI. There was no significant difference between the pts regarding CS, bulky disease and PS. Progression free survival (PFS) after 3 yrs was 84.0% and it was not influenced by CS, bulky disease and PS. PFS was better in pts <60 yrs and pts with low/low intermediate IPI (p=0.035). OS after 3 yrs was 91%. No difference between the subgroups regarding CS, IPI, PS and the presence of bulky disease was found.

Conclusion: Higher rate of CR as well as better 3 yrs PFS were achieved in younger pts (<60 yrs) and in pts with low/low intermediate IPI. According to SLG experience immunochemotherapy showed significant improvement of the outcome of newly diagnosed DLBCL pts. CS, bulky disease and PS haven’t the predictive value on the outcome, so new parameters need to be tested for predictive scoring system.

474 REDUCTION RATE OF ABSOLUTE LYMPHOCYTE COUNT AFTER R-CHOP MAY ESTIMATE SURVIVAL IN PATIENTS WITH EARLY STAGED-DLBCL

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Background: Although the International Prognostic Index (IPI) or absolute lymphocyte count (ALC) was known as a prognostic factor in DLBCL, those have not been confirmed in the rituximab era. We evaluated prognostic factors for survival in patients with early staged-DLBCL after R-CHOP treatment.

Methods: From Aug. 2003, 77 patients with early staged DLBCL, who finished R-CHOP as scheduled according to NCCN guidelines, were retrospectively reviewed. Survival analysis were performed according to clinical parameters (age, performance status, LDH, extranodal involvement, stage, ALC, and difference rate of WBC or ALC).

Results: Among 77 patients with early staged DLBCL 25 patients (32.5%) were classified as high-intermediate, 49 (63.1%) as low-intermediate and 3 (3.9%) as low-risk group. The overall response rate was 100% including 94.8% complete response (CR). Survival analysis demonstrated that a difference rate of ALC after the 1st R-CHOP treatment was the only factor associated with progression-free survival (p=0.049) and response duration (p=0.049), whereas age was the single most important prognostic factor for overall survival (p=0.014).

Conclusion: Although there might be some limitations, our data showed the strong prognostic value of the difference of ALC on survival after R-CHOP treatment. Because ALC is simple to perform as a routine test, the evaluation for difference of ALCs after R-CHOP will be warranted.

475 CLINICAL CHARACTERISTICS AND SURVIVAL ANALYSIS OF LB L Patients TREATED WITH CHOP-BASED REGIMENS ALONE OR WITH CONSOLIDATION HIGH DOSE TREATMENT AND HSCT

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Purpose: Retrospective analysis of the clinical characteristics and survival of lymphoblastic lymphoma (LBL) patients treated with CHOP-based regimens alone or followed by consolidation high-dose treatment and hematopoietic stem cell transplantation (HDT-HSCT).

Experimental Design: From 1999 to 2004, a total of 63 patients with LBL were treated with at least 2 cycles of standard CHOP-based regimens as initial therapy in our Hospital. Among the 63 patients, 26 received consolidation HDT-HSCT, including 23 autologous and 5 allogeneic HSCT.

Results: The median age of the 63 patients was 20 years old. Fifty-seven (90%) cases were diagnosed of T-LBL/ALL and 6 (10%) were B-LBL. Fifty-six (88%) patients had stage III–IV diseases. Bone marrow involvement presented in 18 (29%) patients. Nine (14%) had central nervous system involvement. With a median follow-up of 24 months, the estimated 5-year overall and disease-free survival rates of the 63 patients was 31% and 29%, respectively. For the patients received HDT-HSCT as consolidation therapy, the 5-year OS rate was 59.8% compared with 18.0% for patients treated by CHOP-based regimens alone (p=0.0224). Bone marrow involvement, age 20 years, and primary refractory disease were factors significantly associated with poor outcome. Among the 18 patients with bone marrow involvement, only 3 patients that received allogeneic HSCT were still alive at the follow up time of 22, 32 and 37 months respectively.

Conclusions: LBL patients treated only with short term CHOP-based regimens are insufficient. Addition of HSCT as consolidation therapy and allogeneic HSCT could be treatment option for different patient subsets.

Key words: Lymphoblastic lymphoma; CHOP regimen; stem cell transplantation

476 OBSERVATIONAL STUDY OF DIFFUSE LARGE B CELL LYMPHOMA PATIENTS WITH HIGHEST IPI RISK: PROGNOSIS AND THERAPEUTICS

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Introduction: In order to improve the prognostic evaluation and the therapeutic approach to DLBCL patients with high intermediate to high age-adjusted IPI (aliPI), a research project was designed for the analysis of immunohistochemical markers and the role of autologous stem cell transplantation (ASCT) in first complete remission (CR) for this group of patients.

Material and methods: The impact of the expression of CD10, Bcl-6, MUM-1 and Bcl-2 markers on complete remission (CR), disease-free survival (DFS) and overall survival (OS), either individually and according to cell origin was evaluated by means of immunohistochemistry. Eighty-two patients aged under 60 years old were assessed, of which 16 (19.5%) underwent ASCT in first CR and were compared to patients receiving conventional chemotherapy and being monitored after CR.

Results: Immunohistochemistry was assessable in 75 cases, 24 (32.9%) being classified as GC-type and 49 (67.1%) as NGO-type, with no survival difference between the two groups. Bcl-2 expression was found in 37% (27) of the patients and was the single independent predicting factor of OS prognosis according to multivariate analysis. A significant tendency of expression of this protein was also observed for achieving CR, which was essential for longer survival, as shown by multivariate analysis. OS and DFS within 5 years were of 75% and 85.2% respectively for the group of 16 patients treated with ASCT, which resulted in lower relapse rates (6.5%) with statistically significant difference for DFS (p=0.015) when compared to the group of patients who achieved CR and was kept under monitoring.

Conclusions: In this study ASCT was found to be a safe procedure for improving survival rates of DLBCL patients with high intermediate to high aliPI risk. Also, the expression of Bcl-2 protein was found to be useful as one of the variables to be analysed in the therapeutic approach to these patients.
477 MORPHOIMMUNOLOGIC AND CLINICAL CHARACTERISTICS IN TREATMENT OF PATIENTS WITH DIFFUSE LARGE-CELL LYMPHOMA (DLCL) ASSOCIATED WITH HEPATITIS C VIRUS (HCV) INFECTION

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Background: Several studies have suggested an association between HCV and B-cell DLCL. Treatment and outcome of pts with DLCL and HCV infection are still a matter of debate.

Materials and Methods: Analysis of clinical data and efficacy of treatment has been performed according to CHOP scheme including 25 pts with DLCL and HCV infection (group 1st) and 41 pts with DLCL without HCV infection (group 2nd). Median value of age of pts of the 1st and 2nd was 47 and 63 y.o., respectively. The present disease stages III and IV in the 1st and 2nd at a point of diagnosis was observed in 83% and 52% of pts, respectively. LDH level was increased in 65% of pts of 1st and in 45% of pts of 2nd. Spleen damage in 1st was found in 65% of pts, and in 2nd - in 41% (P<0.05). ALT above the norm in 88% of pts in 1st, and in 46% - in 2nd. In morphologic study plasma differentiation of tumor cells with significant of basophilia of cytoplasm cells were observed in 92% of pts in 1st and 2nd in 8% of pts. Morphoimmunologic study founded that in 92% of pts in 1st there was a positive reaction to proteins and RNA of HCV in tumor cells.

Results: Complete remission was reached in 64% of pts in 1st and in 76% - in 2nd (P>0.05). Median value of even free survival in 1st was 7 months, and in 2nd - 24 months (P>0.02). Recurrence in 1st was noted in 92% of pts, and in 2nd - in 37% of pts. Median value of total survival in 1st was 21 months, and in 2nd - 43 months (P=0.05). After taking courses of chemotherapy cytopenia of 3-4 stages in 1st was founded in 76% of pts, and in 2nd – in 12% of pts.

Conclusion: The study demonstrates: pts with HCV-associated DLCL differ from the patients with DLCL without HCV by clinical, morphoimmunologic of tumor, efficacy and tolerance of chemotherapy. It is required to conduct a specific research which would combine chemotherapy and antiviral therapy as well for these pts.