LYMPHOMA (DLBCL)

PROGNOSTIC FACTOR FOR SURVIVAL IN DIFFUSE LARGE B CELL LYMPHOMA

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Treatment responses and survival rates are different among patients with diffuse large B-cell lymphoma (DLBCL) which might be related to some novel prognostic markers.

Our aim was to examine if treatment and survival results are influenced by Fcgamma receptor IIIa polymorphism (FGCGRA3) and gene expression profile (GEP).

Between 2007 and 2009 thirty-four newly diagnosed DLBCL patients (19 females, 15 males, mean age: 51.7 years) were treated with R-CHOP-14 protocol in our hospital. Among them, FGCGRA3 polymorphism was examined at the 158 amino acid position with polymerase chain reaction, while GEP including bcl-2, bcl-6, CD10, CD30 and MUM-1 markers was investigated using fluorescence in situ hybridization (FISH).

Considering FGCGRA3 polymorphism, the distribution of genotypes was the following: 7 (20%) VV, 5 (15%) FF and 22 (65%) VF. Treatment responses were not significantly different in the three genotype groups. Event-free survival (EFS) was not favourable in patients bearing the F allele, however, the difference was not significant (p=0.163) and overall survival (OS) rates were almost the same. Examining the gene expression profiles, ten cases (29%) were found to be of germinal center (GC) origin, while twenty-four (71%) patients had lymphoma of non-GC origin. There was no difference in their treatment responses, however OS and EFS rates were more favorable in the GC group (p=0.162).

Our results highlight that the prognostic values of both FGCGRA3 and GEP are still controversial.

441 PERIPHERAL BLOOD MONOCYTOSIS IS AN INDEPENDENT PROGNOSTIC FACTOR FOR SURVIVAL IN DIFFUSE LARGE B CELL LYMPHOMA (DLBCL)

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Background: Peripheral blood monocytosis (PBM) has been reported in some cases of malignant lymphoma but its prevalence in DLBCL is not known. Recent in vitro studies have shown that monocytes can promote the survival of lymphoma cells and gene expression profiling done on lymph nodes have illustrated that monocytes/monocyte like dendritic cells infiltrating the tumor environment, play a major role in enhancing the survival of lymphoma cells, displaying immune suppressive function. Recently, we encountered PBM in some patients with DLBCL who had a rapidly progressive fatal course. This observation and the recent emerging data regarding the stromal role of immune cells, led us to undertake a retrospective study to determine prevalence of PBM and its possible prognostic significance in patients with DLBCL.

Patients and Methods: Clinical and laboratory data from the medical records of 91 patients with DLBCL treated in our institute during 1996-2010, were evaluated for the presence of absolute monocytosis, (> 1000 cells/mm3) before treatment and possible correlations with other prognostic factors: B symptoms, age, stage, gender, extra nodal involvement, serum LDH and CRP, bone marrow (BM) involvement, and the IPI score. A Cox proportional hazards regression model was used to determine the significance of the prognostic factors in a multivariate analysis.

Results: Median follow up was 30 months (1-352 months) and PBM was found in 18.3% of patients at presentation. In the univariate analysis, PBM, IPI score, stage, LDH, and BM involvement were all associated with a worse prognosis. In the multivariate analysis (Cox model), only PBM, BM involvement and IPI were found to be independent prognostic factors for overall survival (os).

<table>
<thead>
<tr>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>Pr &gt; ChiSq</th>
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<tbody>
<tr>
<td>IPI</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>MONO &gt;1000</td>
<td>1.154</td>
<td>8.475</td>
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<tr>
<td>BMInvolved</td>
<td>1.487</td>
<td>9.757</td>
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Conclusions: This study indicates that PBM is an independent prognostic value associated with poor prognosis and os in patients with DLBCL. This easily applied routine laboratory test can be readily utilized and potentially significant results can be quickly obtained. We recommend that it be considered as a simple additional indicator of poor outcome in DLBCL. These findings provide further support for the importance of monocytes and their functional role in the immune response in DLBCL. Studies on their involvement in the biology of DLBCL are now in progress in our laboratory.

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445 SAFETY, EFFICACY AND PHARMACOECONOMIC ANALYSIS (PA) OF RAPID INFUSION (RI) OF RITUXIMAB WITHOUT INFUSION PUMP (IP) IN NON-HODGKIN LYMPHOMAS (NHL): EXPERIENCE OF A BRAZILIAN PUBLIC HOSPITAL


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Introduction: Rituximab, a monoclonal chimeric anti-CD20, has been widely used in the management of NHL even in patients in the National Health System (NHS). The increase in the use of this monoclonal antibody (MAb) in the treatment of NHL with a long infusion time (standard infusion-SI) is resulting in overload of chemotherapy services primarily concentrated in the NHS where most patients undergo treatment. The RI of rituximab after the second dose for 90 minutes with IP seems to solve this problem. Objective: evaluate the characteristics of patients with NHL who received RI of rituximab without IP at Santa Marcelina Hospital as well as efficacy, safety and PA of the RI of rituximab.

Material and Methods: We retrospectively evaluated 51 patients with NHL who received RI of rituximab between April 2009 and January 2011. The diagnosis of NHL was based on histopathological analysis and immunohistochemistry of biopsy. We used Ann Arbor staging and International Prognostic Index (IPI) for prognosis and the NCIW group criteria to assess response. The criterion of NC1 during reactions infusions of MA to assess toxicity was used. The Kaplan-Meier method to evaluate overall survival (OS) and progression-free survival (PFS) was also used. The EXCEL program projected the number of additional type R-CHOP chemotherapy that would be performed by reducing the infusion time for the introduction of RI and the economy of this protocol by subtracting the values passed on by the NHS versus total expenditure (drugs, supplies, fees).

Results: 30 patients were male and 21 female, average age of 59 (20-82). Of the 51 cases of NHL, 34 were aggressive and 17 indolent with Ann Arbor stage I, II (14) and III, IV (37), low IPI in 11 patients, intermediate in 37 and high IPI, 192 RI of rituximab were performed with an average of 3.8 per patient and a mean follow-up of 38 months. We observed only 2 cases of mild reactions and 4 deaths where 3 of them were related to the treatment. Of the 51 patients evaluated, 86% had CR corresponding to 83% of 88% and PFS of 80%. PA found that 16 cases would be treated more in this new period using RI of rituximab with an economy of US $55,099.67 to the transfers of NHL.

Conclusion: The RI of rituximab without IP was safe, with high rates of CR, OS, PFS and pharmacoeconomic advantage compared to SI. Moreover, for the first time ever in literature it was found that a RI of rituximab has a similar efficacy to SI. These results certify the use of RI of rituximab as standard protocol in patients with NHL particularly those treated by the NHS.

446 COMPREHENSIVE SYMPTOM PROFILE IN PATIENTS WITH MALIGNANT LYMPHOMAS: PRACTICABILITY AND SENSITIVITY OF THE NEW SYMPTOM ASSESSMENT TOOL CSP-LYM

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Symptom profile and severity is one of the important treatment outcomes in patients with malignant lymphomas. Comprehensive symptom assessment and monitoring before and during treatment as well as follow-up is worthwhile. Recently a new tool, Comprehensive Symptom Profile in Lymphoma Patients (CSP-Lym), has been developed to assess symptoms specific for patients with malignant lymphomas. We aimed to test practicability and sensitivity of CSP-Lym. A total of 106 patients with different types of malignant lymphomas (Stage – II–IV) were included in the study: non-Hodgkin’s lymphoma–45; Hodgkin’s lymphoma – 61. Mean age was 34.8 years old (20-82). Seventy female distribution: 85 patients (79.7%). MFC at CR relapsed compared with 8 of 32 with a negative test (p=0.83); 4 of 4 with a positive MFC at EOC relapsed compared with 4 of 22 with a negative test (p=0.101). Among patients with available BCR-ABL results at CR, 7 of 25 patients with a MMR (BCR-ABL<0.1%) at CR relapsed compared with 10 of 31 with less than MMR (BCR-ABL>0.1%) (p=0.73); 3 of 6 patients with MMR at EOC relapsed compared with 17 with 14% MMR at EOC.

Conclusions: A positive MRD by MFC at EOC is associated with a higher likelihood of relapse but achieving MMR at EOC does not protect against relapse. This data may help in devising risk-adapted therapy in patients with Ph+ ALL.
Background: Recent studies divided diffuse large B-cell lymphoma (DLBCL) into germinal center B-cell like (GCB) and non germinal center B-cell like (non-GCB) subgroups, which showed prognostic significance. The addition of rituximab to chemotherapy brought survival benefit in both subgroups.

Patients and Methods: We studied 99 patients with de novo DLBCL treated with R-CHOP 21 immunochemotherapy. The patients were obtained from Serbian National Lymphoma Register (the enrollment started from April 2008). The division to GCB and non-GCB subgroups was made based on immunohistochemical findings by using the Hans method. The baseline characteristics that were correlated with immunophenotype were age, sex, IPI score, Ann Arbor Clinical Stage, ECOG performance status, presence of B symptoms, bulky disease, extranodal disease, spleen enlargement, number of involved lymph node areas, bone marrow involvement, ESR, LDH level, β2-microglobulin, CRP, Hgb level, WBC count, platelets count, total serum proteins and albumin. Also, bcl-2 expression and different levels of Ki-67 expression were correlated.

Results: Thirty patients (30.3%) expressed GCB phenotype. In our analysis, there was no difference regarding the complete remission (CR) rate. The only difference in Ki-67 and Kiesselbach3, L. Trumper1 were correlated.

Conclusions: The addition of rituximab to CHOP 21 immunochemotherapy. The patients were obtained from Serbian National Lymphoma Register (the enrolement started from April 2008). The division to GCB and non-GCB subgroups was made based on immunohistochemical findings by using the Hans method. The baseline characteristics that were correlated with immunophenotype were age, sex, IPI score, Ann Arbor Clinical Stage, ECOG performance status, presence of B symptoms, bulky disease, extranodal disease, spleen enlargement, number of involved lymph node areas, bone marrow involvement, ESR, LDH level, β2-microglobulin, CRP, Hgb level, WBC count, platelets count, total serum proteins and albumin. Also, bcl-2 expression and different levels of Ki-67 expression were correlated.

449 WITHDRAWN

450 PHARMACOKINETICS OF RITUXIMAB IN COMBINATION WITH CHOP-14 AND CHOP-21 CHEMOTHERAPY IN DLBCL

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Background: Because of the scarcity of data in diffuse large B-cell lymphoma (DLBCL), rituximab pharmacokinetics in combination with CHOP-14 and CHOP-21 was studied in patients with DLBCL.

Material: Serum rituximab levels were investigated in 36 patients who were treated at different centers participating in the prospective multicenter UNFOLDER trial of the DSHINH (NCT00729408), where in a randomized fashion an immunomunotherapy with 6 cycles of rituximab in combination with 6 cycles of chemotherapy with CHOP at 21-day intervals or 14-day intervals were compared, both with or without consolidating radiotherapy to bulky disease (≥7.5 cm) and/or extranodal involvement in patients with proven aggressive CD 20 positive B-Cell Lymphoma aged 18 to 60 years with age-adjusted IPI=1 (all) or IPI=0 with bulky (≥7.5 cm). Ten minutes before and ten minutes after the rituximab infusion in each immunomunotherapy cycle, 10 mL of blood were drawn from each subject to obtain rituximab trough and peak (data not shown) levels. Additional samples were taken 1 month, 2 months, 3 months and 6 months after the last rituximab infusion. Rituximab serum levels were determined by Xendo Laboratories, Groningen, NL by an enzyme-linked immunobioassay assay.

Results: Eighteen patients were included in pharmacokinetic analysis of each arm of the trial. 2 week- application of rituximab showed a more rapid increase of serum rituximab levels (day 70 vs. 135) and higher maximal levels (125 pg/mL vs. 95 pg/mL) compared to the standard 3-week protocol (see Table 1). Surprisingly, despite the fact that the last application of rituximab in the 2-week regimen was given in week 10 compared to week 15 in the 3-week regimen, the rituximab serum levels in the 2-week regimen persisted as long as those in the 3-week regimen.

Conclusion: 2 week application of rituximab is associated with a more rapid increase of serum rituximab levels and higher maximal levels, while rituximab serum levels are maintained as long as in the 3-week regimen. This results in a greater area under the curve for the 2-week regimen compared to the 3-week regimen. Longer follow-up is needed to see whether the greater area under the curve is associated with better results for R-CHOP-14 over R-CHOP-21 in this randomized trial. The results of this study serve as a basis for future protocols aiming at optimizing the use of rituximab in DLBCL.

451 RADIOIMMUNOTHERAPY FOR CONSOLIDATION AND RELAPSE TREATMENT OF AGGRESSIVE B-CELL NON HODGKINS LYMPHOMA: AN UPDATED ANALYSIS OF THE INTERNATIONAL RIT-NETWORK

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Radioimmunotherapy (RIT) for lymphoma with labelled anti-CD 20 antibodies has shown high response rates and durable remissions in extensively pretreated patients (pts). In aggressive lymphoma, data are sparse, and studies with RIT as consolidation and relapse are ongoing.

Data of pts with DLBCL registered in the international RIT-Network (RIT-NT) were analyzed with regard to Indication, line of therapy and outcome. The RIT-NET is a web-based registry that collects observational data from RIT-treated patients with malignant lymphoma from across the world.

232 patients with DLBCL were evaluated in the following analysis. 232 pts with DLBCL are registered, 17 pts had to be excluded. Histologic subtypes: 190 diffuse large B-Cell, 15 primary mediastinal, 9 large cell anaplastic, 1 intravascular. Median age 62 years (range 17-88), 27% > 70 years old. Stage: 1: 16 pts, II 54 pts, III 60 pts, IV 68 pts; 6 extranodal involvement, for 11 pt. stage is not documented. 187 pts had hist 1-3 previous chemotherapies (Ctx), 21 pts 4-6 previous Ctx, 1 pt had seven previous Ctx, for 6 pts previous Ctx is not documented. 15 pts had previous RIT and 24 pts a stem cell transplantation prior to RIT. 6 pts had bone marrow infiltration prior to RIT, with infiltration of more than 25%, 87 pts had RIT as first line (8 pts as part of the conditioning, 68 pts consolidation, 1 primary therapy, 10 other) and 84 pts received RIT in relapse (2d to 8 th. line therapy) (2 pts as part of the conditioning, 31 pts consolidation, 26 recurrence, 19 therapy refractory, 6 other). Grade IV Haematotoxicity occurred for neutrophils and platelet, grade III+ for haemoglobin after RIT. Median time to recovery of blood count was 81 days (range 0-680 days). Overall response rate was 60%; CR 30%; PR 10%; SD 1%; PD 26%; N.D. 15%. CR rate for first line pts was 75%, for relapse 37%. Mean overall survival (OS) in first line therapy was 788 and 446 days for pts treated in relapse or refractory disease.

Most pts with DLBCL receive RIT as consolidation after first line therapy with excellent CR rates and OS. Also for pts in relapse RIT is a safe and feasible treatment leading to satisfactory response rates with a low toxicity. Especially in elderly pts RIT should continue to be explored in prospective clinical trials.

452 PHASE 2 STUDIES OF IMMUNOCHEMOTHERAPY ± BORTEZOMIB (VC) IN NEWLY DIAGNOSED NON-GERMINAL CENTER B-CELL-LIKE (GCB) DLBCL: RAPID PROSPECTIVE IDENTIFICATION OF NON-GCB PATIENTS (PTS)


Introduction: LYM2034 (non-US) and PYRAMID (US) are prospectively enrolling pts with non-GCB DLBCL, which has inferior outcomes vs GCB DLBCL following R-CHOP. Prior studies suggest Vc has benefit specifically in NF-kB dependent non-GCB DLBCL, consistent with Vc-mediated inhibition of the NF-kB pathway. We report operational aspects of real-time pathology assessments in both studies.

Material and Methods: Pts aged ≥21 yrs with ECOG PS 0–2 are eligible. Non-GCB tumor subtyping is done at a US central laboratory via the Hans IHC assay (CD10-, BCL6-, or BCL6+ and MUM1+). Non-GCB pts are randomized to six 3-week cycles of R-CHOP vs Vc 1.3 mg/m2 (d 1, 4, 8, 11) + R-CHOP (R-CHOP minus vincristine) or Vc 1.3 mg/m2 (d 1, 4) + R-CHOP (PYRAMID). Results: In LYM2034, 167 pts have been screened, 75 identified as non-GCB DLBCL, and 62 randomized. In PYRAMID 100 pts have been screened, 39 identified as non-GCB DLBCL, and 34 randomized. Mean time from receipt of sample to subtype reporting is 5.6 days in LYM2034 and 1.2 business days in PYRAMID; mean time for return of pathology block to clinical site is 2.3 weeks and 4.4 days, respectively. Use of the Hans algorithm are being compared with those using the Choi and Tally algorithms; initial analyses show high concordance.

Conclusions: LYM2034 and PYRAMID demonstrate that prospective enrichment of non-GCB DLBCL pts is feasible with rapid subtype identification. These studies continue to enroll pts.
Background: DepoCyte is a sustained-release formulation of cytarabine, characterised by biphase elimination profile with a terminal phase half-life of 100 to 263 hours over 50 times longer than free cytarabine designed specifically for intrathecal administration.

Materials And Methods: Eighty five patients with aggressive high risk NHL received DepoCyte either as prophylaxis (N=60) or treatment (N=25) of central nervous system (CNS) involvement. In patients receiving prophylaxis, high risk was defined as presence at least 2 of the following: elevated LDH (n=33, 88%), involvement of 2 or more extranodal sites (n=20, 33%), IPI 3-5 (n=36, 61%) and specific lymphoma localizations (testis, vertebral column, orbits, sinuses, bulky mediastinal tumor; n=36, 60%). None of the patients had neurological symptoms at diagnosis, nor any abnormalities in imaging studies or cerebrospinal fluid analysis (average cellularity 2.5 x 10^3/mm³, range 0-9). In the treatment subgroup, disease was confirmed by CNS fluid cytology in 18/25 (72%) patients (average cytosis 128, range 19-650) and/or imaging studies (20/25, 80%) at diagnosis (n=15, 60%) or at relapse (n=10, 40%).

Results: In prophylaxis DepoCyte 3.4 doses (2-6) were administered at a time of chemotherapy cycles or after treatment finishing necessity (18 patients (n=47) or 3(n=13) weeks). At medium observation duration of 14 (1-32) months 54/60 (90%) patients were alive, without CNS relapse. Only 2 (3.3%) cases relapsed (a systemic/CNS relapse in lymphoblastic lymphoma and isolated CNS relapse in DLBCL patients after 8 and 18 months respectively). Treatment of CNS disease consisted of 4.6 doses (1-8) with concomitant chemotherapy in 57 % and subsequent radiotherapy in 52% of cases. The median OS and EFS were 33 months and 20 months respectively.

Conclusions: In prophylaxis DepoCyte proved to be an efficient, convenient and well tolerated drug reducing number of relapses in a high risk aggressive NHL to 3.3%. Used in a treatment setting it prolonged response duration and improved quality of life.

454 HEPATIC TOXICITY IN PATIENTS WITH NON HODGKIN'S LYMPHOMA (NHL) INFECTED WITH HEPATITIS C UNDERGOING CHEMOTHERAPY WITH RITUXIMAB

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It’s shown that virus hepatitis C (HCV) is one of etiopathogenic factors of NHL. It’s shown that level of various markers of HCV at patients from NHL can be tapped at 30 % of patients (pts). In literature well-known role of hepatitis B at carrying out immunohistochemistry (IHC). The hepatitis C at IHC is studied little.

In our research we studied function of liver at pts with NHL at carrying out IHC with markers of HCV at them. 64 pts with NHL have been included in research with markers HCV infection and 196 without it by which it has been spent ICT. Pts with HCV infection was 21 pts with indolent lymphoma (IL), 41 diffuse large B cell lymphoma (DLBCL) and 2 with chronic lymphocytic leukemia (CLL). The age median has made 47 years. III-IV stages of disease were at 52 patients, 11 II stage and 1 IIE.

Normal level ALT and AST was at 167 pts. All pts were treated by R-CHOP or R-FC.

Serum level HCVRNA has increased at 39 of 64 pts. At all 39 pts before therapy had positive serum level HCV RNA. Level of HCV RNA was from 3x10⁶ to 8.8x10⁶/ml a median has made 4.2x10⁶/ml. 37 from 64 pts simultaneously with increased serum level HCV RNA increased level ALT and AST. Level ALT was from 2 to 50 norms. median- 7.5 norms. Level AST increased at 43 pts from 2 to 10 norms, median of 4.5 norms. The reason of stop treatment at 19 pts was hepatic toxicity. Complete remission (CR) in Pts with HCV infection has been reached at 14 about IL and 12 DLBCL. Median follow up was 12 months.

Among 196 pts without HCV infection increased level ALT and AST only at 15 pts. Median was 2.3 norms. HCV RNA was not defined at all this 15 pts. The treatment has not been stopped as thanks to hepatic toxicity. CR has been reached at 28 about IL and 56 with DLBCL. Median follow up was 28 months.

Significant proportion of patients with HCV + NHL develop liver toxicity often leading to interruption of treatment. This could be limited to the application of immunochemotherapy programs. HCV + lymphomas represent a distinct clinical subset of NHL that deserves specific clinical approach to limit liver toxicity and survival.

455 A STUDY COMPARING METHODS OF ASSESSING CARDIAC DAMAGE IN TREATED LYMPHOMA PATIENTS

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Background: Heart disease is the most common non-malignant cause of morbidity and mortality among lymphoma survivors. Anthracycline chemotherapy can contribute to heart muscle damage while radiation may affect pericardium, myocardium or coronary vasculature. Combined modality therapy is thus especially likely to confer late cardiac damage. Attempts to screen for heart disease have focused on use of echocardiograms but it appears this is not sensitive in detecting early signs of damage. Serum BNP (brain natriuretic protein) is used increasingly in cardiology to screen populations and has been shown to be a reliable predictor for damage. The gold standard for assessing function is cardiac magnetic resonance. We designed this study to determine whether serum BNP might suffice as an early marker for damage, comparing against cardiac MR and echo in late survivors of combined modality therapy for lymphoma.

Method: 20 patients were recruited for cardiac screening. All had completed combined modality therapy for lymphoma more than 8 years previously, were currently in remission and did not have known heart disease or significant risk factors other than previous therapy. Each completed risk questionnaire, and had ECG, echocardiogram, cardiac MR and serum BNP checked.

Results: 5 men, 15 women were recruited. Age range at time of study 25-58 years (median 40) with time since last treatment of 8-20 years (median 10). 5 patients had DLBCL and 15 Hodgkin’s (HD), with 7 of the HD having had relapses and further treatment. Radiotherapy doses ranged from 30-45 Gy. Five patients had mantle radiotherapy. Adjuvant CT doses of 150-450mg/m² were given. 4 patients were ex-smokers with 3 current smokers. Echocardiogram in all was reported as normal, as was ECG. Serum BNP results also were within normal range. Cardiac MR detected clear signs of reduced ejection fraction in 5 patients who were referred on to cardiology department.

Conclusion: As expected echocardiogram did not detect reduced cardiac function in asymptomatic patients. Our hypothesis that serum BNP might identify these patients has not been confirmed. Cardiac MR however does detect early changes ahead of other methods. We intend to further evaluate the cardiac MR with respect to coronary arteries, sites of cardiac damage and relation to radiotherapy fields.

456 THE IMPACT OF ADDITION OF RITUXIMAB TO CHEMOTHERAPY ON INCIDENCE OF CENTRAL NERVOUS SYSTEM RELAPSE IN PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA

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Introduction: The addition of rituximab to CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) was proved to improve remission rate, event-free and overall survival of patients with diffuse large B-cell lymphoma (DLBL). We evaluated the impact of rituximab on the incidence of central nervous system (CNS) relapse in the DLBL in Hong Kong.

Method: Patients aged 18 or above with DLBL patients diagnosed from January 1997 to December 2009 were identified. They were recruited into the study if they were treated with CHOP or R-CHOP with curative intent. They had a minimum follow-up of 12 months. CNS involvement was defined as either the presence of malignant lymphoma cell in the cerebrospinal fluid (CSF) or typical imaging result in magnetic resonance imaging or computerized tomography. The rate of CNS relapse was compared in the two groups. Incidence and risk factors for CNS relapse were also identified.

Results: A total of sixty-nine patients were recruited in the study. Thirty-six patients (52%) received CHOP and thirty-three (48%) received R-CHOP. The baseline characteristics of the two groups were similar. The median age was 55 and 49 in the CHOP and R-CHOP groups respectively. There were a total of seven CNS relapse with incidence 10.1% in the study. The incidence of CNS relapse was 11.1% in the CHOP group and 9.1% in the R-CHOP group. There was no significant difference between the groups.

The significant risk factors identified for CNS relapse included stage IV disease (p=0.001, Fisher’s exact test), bone marrow involvement with lymphoma (p=0.019), and lactate dehydrogenase (LDH) level three times above upper limit (p=0.019).

Conclusion: The addition of rituximab did not appear to decrease the risk of CNS relapse in patients with diffuse large B-cell lymphoma in this study.

457 RITUXIMAB, GEMCITABINE AND OXALIPLATIN (R-GEMOX) IN THE TREATMENT OF RELAPSED OR REFRACTORY LYMPHOMA: THE EXPERIENCE FROM A SINGLE CENTRE

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Introduction: The treatment of relapses of non-Hodgkin Lymphoma (NHL) in the era of Rituximab (R) is very difficult. Most of the regimens available are remarkably toxic.
requiring hospitalization with each combination of treatment with the combination of R with Gemcitabine (GEM) and OxaPlatin (OX), we decided to study a new open phase II trial, including all NHL CD20+ refractory and/or relapsed, to determine the efficacy, toxicity, the possibility of harvesting hematopoietic progenitors and the feasibility in an outpatient basis.

Methods: We treated from JAN 09 to DEC 10 refractory and relapsed NHL CD20+ with R-GEMOX: R-375mg/m2iv, D1; GEM-1000mg, infusion rate of 10mg/m2/min, iv; D2; OX-100mg/m2, iv, D2,14/14 day cycles, maximum of 6 cycles. We treated 21 patients, 13 woman, median age of 64 years (range 25-76), median time from diagnosis of 25 months (range 1-144), Type (Diffuse/11; Follicular/3; Mantle Cell/4); Lymphoma/3; Small/4; Others/1). Ann-Harbor (I/11; II/4; III/6; IV/10), IPI (1/3; 2/5; 3/5; 5/2), FLIPI (1/2; 1/2; 3/1), MPII (1/2; 2/2), ECOG (0/5; 1/14; 2/2); dose reduction in 1 patient and lowering the perfusion rate in the other 3; Eight infective complications, 6 respiratory with only one hospitalization. We performed 6 autologous stem cell transplant and 1 allogeneic. The median time of follow-up was 6M (range 2-21M). 6 patients received PD, 1 with severe respiratory infection and 1 for Pulmonary Aspergilllosis and GVHD after allogeneic transplantation. The remaining patients with PD are in rescue treatments.

Conclusions: The R-GEMOX was feasible in ambulatory regimen with acceptable toxicity, allowed the harvest of hematopoietic progenitors in all proposed patients (5) and had an appreciable efficacy if we consider the characteristics of patients included (Overall Response = 47.6%).

458 TUNISIAN EXPERIENCE IN THE TREATMENT OF AGGRESSIVE NON HODGKIN’S LYMPHOMA IN ADULTS: ABOUT 337 PATIENTS

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Introduction: Diffuse large B-cell lymphoma is the most common type of non- Hodgkin’s lymphoma (NHL). Median age at diagnosis is 65 years, up to 35% of patients are older than 70 at diagnosis. Identification of suitable treatment options for older patients is assuming greater interest.

Recent studies show the best way to improve survival of older patients is to administer an optimal chemotherapy regimen, and first line CHOP and Rituximab is now the gold standard for aggressive lymphomas in older patients. Few series have been dedicated to the treatment of relapsing older patients. In most series the upper age limit is 65-70 and outcome of the elderly is not specifically mentioned. In this study we retrospectively review the clinical features, treatment and outcome of patients older than 70 with relapsed or refractory disease that received conventional salvage regimens.

Methods: Records of patients older than 70 with NHL and treated in 2000-2009 were retrospectively review the clinical features, treatment and outcome of patients older than 70 with relapsed or refractory disease included. Chemotherapy given, dose intensity, complications and response were recorded. Second line protocols were divided into aggressive (platinum- based) and non aggressive (all others).

Conclusions: Outcome was defined by complete remission (CR), time to progression (TTP) and Overall survival (OS).

Results: 32 patients were included. Median age was diagnosis was 72. 1st line chemotherapy was CHOP in 43.8% and R-CHOP in 34.4%. CR rate was 71.9%. 10/32 patients were refractory to 1st line chemotherapy. Median time to 1st relapse was 24.5 months and median age at 1st relapse was 74. All patients received at least one line of salvage. 96.9% received aggressive chemotherapy. CR rate after 2nd line chemotherapy was 40.6%. Median time to 2nd relapse was 31.3 months. CR rate was 42.3% in patients receiving aggressive chemotherapy and 33.3% in those receiving non aggressive regimens. Patients receiving an aggressive protocol had longer TTP- 42.2 months vs. 18.7 months. Median OS was 32 months. Most common complications were sepsis and neutropenic fever. 40.6% and 59% of patients were hospitalized due to complications after 2nd and 3rd lines of chemotherapy respectively.

18/32 patients died- 2 due to sepsis and 16 due to Lymphoma progression.

Conclusion: Salvage therapy for refractory/ relapsed aggressive lymphoma in elderly patients is feasible. 42.3% of patients achieve a 2nd CR with median TTP of 42.2 months and median OS of 32 months.

The best way to improve outcome of elderly patients with relapsed/refractory aggressive lymphoma is to administer the same salvage therapy as younger patients.

461 RITUXIMAB IMPROVES QUALITY OF RESPONSE AND SURVIVAL IN ELDERLY PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL): A POPULATION-BASED STUDY

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Introduction: CHOP-rituximab has become the standard of treatment of DLBCL. However, whether these results are reproducible in our daily practice is still a matter of interest. We decided to analyse the outcome of patients over 65 treated at our institution with conventional chemotherapy compared with those receiving rituximab combined regimens.

Methods: We included 106 patients consecutively diagnosed of DLBCL at our institution between January 1990 and June 2010 who received active treatment. Median age was 74 years (range, 65 to 96), Male sex 46 (42%), Bulky disease was present in 43 (39%), PS2, 34 (31%), Ann-Arbor stage II 125 (23%), III (30%), II (28%), IV (27%), increased LDH 46 (43%), increased beta-2-microglobulin (UNL) 40 (36%), ≥ 1 extranodal sites 14 (13%) and IPI ≥ 2, 43 (39%), 61 (56%) patients received...
conventional chemotherapy with anthracycline-containing regimens (group A) whereas 45 (41%) patients were treated with a rituximab-containing regimen, mainly CHOP-R (group B). Major characteristics of both cohorts (pre and postrituximab) did not show statistical significance except for LDL levels which were higher in the rituximab-treated cohort (A: 32% vs B: 61%, p=0.005).

Results: Median follow-up of the alive patients was 45.7 months (0.8 to 157.3), 76 out of 103 (74%) achieved a complete remission, 41 out of 58 (71%) in rituximab-naive patients and 34 out of 45 (77%) in the rituximab-treated ones. Median time to progression (TPP) was 49 months (95%CI 24.73) in group A and not reached in group B. Median overall survival was 60.75 months 95%CI (20.4, 101.1) in group A and 92 months (67.1, 117) in group B (p= 0.09). Considering lymphoma-specific mortality, 68% of group A were alive at 48 months compared to 91% (p=0.01) of group B. Main clinical variables identified in multivariable analysis for TPP and survival were treatment with rituximab (HR 0.2 95% CI 0.07, 0.52) and (HR 0.16 95%CI (0.04, 0.69) respectively (p=0.001), and iPI score ≥ 3, HR 2.59, (1.28, 5.23) and3.33 (1.24, 8.92) (p=0.008).

Conclusions: In our experience, rituximab in combination with chemotherapy improves the quality of response and both, overall and lymphoma-specific survival in our elderly lymphoma population. Combination of CHOP-rituximab allowed to complete the whole course of treatment compared to more intense chemotherapy schedules previously used.

462 RARE FORMS OF PRIMARY EXTRANODAL NON-HODGKIN’S LYMPHOMAS: DISTANT RESULTS AFTER 1 LINE THERAPY (EXPERIENCE OF ONE RUSSIAN CENTER)

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Abstract: Extramodal NHL is rare disease (1.1%-10% of all NHL). The aim of our review was determination and comparing of distant results after 1 line therapy of several type rare extramodal NHL: thyroid, parotid, tests, bone.

Materials and Methods: 708 patients with primary extramodal NHL were observed in CRC of RAMS from 1983 to 2007. More rare forms in 235 cases (33% of all extramodal NHL) were exposed by us, diagnosis was determined after ectomy, resection or open biopsy of the tumor with following immunohistochemical method investigation.

Results: 39 patients (16,6%) were affected by primary NHL of thyroid gland. Median of follow-up 59 months (mnts). Histological type: diffuse large B-cell lymphoma (DLBCL) - 27 (69.2%) pts. Early stages - in 61%; IE-28%, III-13%. Therapy: CHOP +/- R-21 - 24 cases (61,5%), chemotheramodotherapy (summary dose - 34-38 Gy) - 8 (20,5%). Median of overall survival (OS) - 38 mnts. OS: 1 year-79%, 3 year - 52%, 5 year - 37%.

Conclusion: Disease free survival (DFS): 1 year - 57%, 3 year-52%, 5 year-25%. Parotid gland NHL 44 cases (18,7%). Median of follow-up - 74,2 mnts. Histological type: DLBCL-41%, MULT lymphoma- 39%. Early stages in 66%: IE-34%, IIIE-34%. Therapy: CHOP+/+ R-21 - 29 (66%), chemotheramodotherapy (SD 34-42 Gy) - 16 (36%), median of OS -91 mnts. OS: 1 year-92%, 3 year - 80%, 5 year-71%. DFS: 1 year-88%, 3 year-74%, 5 year-47%. NHL of tests - 62 pts (26%). Median of follow up - 30 mnts. DLBCL-66% (97%). Quantity of early and advance stages were the same: IE-35.5%, III-15.4%, III-19.3%, IV-30.76pts.

Therapy: CHOP+/+ R-21 - 40 (64,5%), chemotheramodotherapy (SD 44-60Gy) - 6 (9%). Median of OS 18 mnts. OS: 1 year - 67%, 3 year - 29%, 5 year - 17%. DFS: 1 year - 48%, 3 year-32%. Cases of bone-tumors 38% cases. Median of follow-up - 60 mnts. DLBCL - 65 (83,3%). Quantity of early and advance stages the same: IE-41.5%, III-15.4%, III-19.3%, IV-30.76pts.

Conclusion: The favourable prognostic group was lymphoma of parotid gland (median of OS 91 mnts, OS 3 year - 71%, DFS 5 year - 47%), primary lymphoma of tests was delivered to poor prognostic group (median of OS 18 mnts, OS 5 year - 17%, DFS 5 year - 12%).

463 PLATINE AND CYTARABINE-BASED SALVAGE TREATMENT FOR PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

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Abstract: Primary CNS Lymphoma (PCNSL) is an uncommon malignancy with potentially aggressive behavior. To access the management strategies and outcome of PCNSL in routine clinical setting, a retrospective study has been performed in the Department of radiotherapy, a tertiary care institute of north India.

Material and Method: Between January 2004 and May 2010 a total 39 patients of PCNSL were treated. Thirty-two patients had histologically proven while 7 patients diagnosed radiologically. After routine investigations, all patients received WBRT, followed by chemotherapy with CHOP regimen. Bi-weekly intrathecal methotrexate was given in patients having CSF spread till it came out to be negative.
466 HIGH-DOSE METHOTREXATE, TEMOZOLOMIDE AND INTRATHecal LIPOSOMAL CYTARABINE (HD-MTX-TMZ-IT LC) WITHOUT RADIOTHERAPY FOR PRIMARY OR SECONDARY CENTRAL NERVOUS SYSTEM (CNS) LYMPHOMA

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Background: CNS lymphoma is an aggressive tumor. Combined systemic chemotherapy-radiotherapy may be associated with acute and/or delayed neurotoxicity. HD-MTX-TMZ appears to be an effective and relatively safe regimen. Adding IT LC may further improve therapeutic efficacy. We report our preliminary experience with HD-MTX-TMZ plus IT LC used upfront or as salvage in 4 CNS lymphoma patients.

Material and Methods: Induction: MTX 3g/ms IV d 1, 10, 20, TMZ 100 mg/ms d 1-5; maintenance (25±pts): MTX 3g/ms d 1, TMZ 100 mg/ms d 1-5; every month up to 5 cycles as long as response was documented. Fifty mg IT LC was given concomitantly, at least 14 days apart and at least 7 days from HD-MTX, up to 6 doses. Results: pt 1, 56 y, male, tectal diffuse large B cell lymphoma (DLBCL), stage IVA, cerebellar relapse after CR, Karnofsky performance status (KPS) 50%, Rituximab-TMZ and IT MTX were initiated but soon discontinued due to CMV pneumonia. After recovery, HD-MTX-TMZ was started and precautionary stem cell harvest performed. Six cycles and 4 IT LC injections were given with no G3-4 toxicities. He obtained CRu. Pt 2 76 y, male, primary CNS peripheral T cell lymphoma not otherwise specified, multicentric, KPS 60%. He was treated with steroids and TMZ, but progressed in 3 months. He received 6 HD-MTX-TMZ cycles with 4 IT LC injections. G2 renal insufficiency and G3 steroid-induced diabetes mellitus were reported. He obtained CR. However, 7 months later he relapsed in involved sites, received 2 further cycles of TMZ and is now in SD. Pt 36 y, female, PCNSL, DLBCL, left cerebellar hemisphere, KPS 50%. HD-MTX-TMZ and concomitant IT LC were initiated as first-line, G3 atrial fibrillation was reported. Maintenance was completed. After the 5th IT LC injection she developed grade 3-4 neutropenia and IT therapy was withdrawn. She obtained very good PR after induction. Pt 4, 71 y, female, DLBCL stage III E (i.e. subcutaneous facial localisation), with multicentric bilateral subcortical relapse. Four HD-MTX-TMZ cycles and 5 IT LC injections have been given so far, with no neurotoxicity. CR was attained after induction and sustained thereafter.

Conclusions: HD-MTX-TMZ-IT LC therapy appeared feasible and effective, even in elderly pts. CR/Cru was attained in 3/4 pts. Response duration was 18+, 7+, and 5+ months in pts 1, 2, 3, and 4 respectively. Conus-cauda equina syndrome is a known complication of IT chemotherapy via lumbar puncture. Follow-up is too short to make comments on delayed neurotoxicity.

467 LONG TERM FOLLOW UP OF LOCALIZED, PRIMARY GASTRIC DIFFUSE LARGE B-CELL LYMPHOMA TREATED WITH RITUXIMAB AND CHOP

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Introduction: Addition of rituximab to cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), i.e. R-CHOP is considered as the standard regimen for treating localized, primary gastric diffuse large B-cell lymphoma (PG-DLCL).

However, few studies reporting the long-term efficacy of R-CHOP therapy in the management of localized PG-DLCL have been published.

Material and method: We performed a retrospective analysis of 14 patients with localized PG-DLCL treated with R-CHOP at Nihon University Itabashi Hospital and Kawasaki Medical School in 1999. Limited cases characterized as stage I/II according to the Lugano staging system for gastrointestinal (GI) lymphomas.

Result: The median age of patients was 68 years (range 48–82). Gastralgia and anemia were common symptoms at initial presentation. All patients except 1 received 6 cycles of R-CHOP treatment without consolidation radiation therapy or prior surgery. All patients achieved complete remission, and the estimated overall survival with a median follow-up of 46 months (range 7–92) was 100% without relapse or significant GI adverse effects such as perforation or bleeding during R-CHOP treatment. No long term adverse effects of rituximab were recorded during the observation period. Helicobacter pylori infection was diagnosed in 78.5% of patients, but was eradicated in a limited number of patients.

Conclusions: Our results illustrate the feasibility and effectiveness of the addition of rituximab to conventional CHOP therapy in the management of localized PG-DLCL.

468 PRIMARY EXTRACRANIAL LYMPHOMAS OF LIVER (PELL): CLINICAL, DIAGNOSTIC AND TREATMENT

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PELL as the primary tumour meets seldom. In literature all PELL was non Hodgkin’s lymphoma (NHL). PELL is 0.4% of all NHL. Diffuse B-cells lymphomas (DLBCL) composed to 96% of all PELL. At 60% of patients PELL has one solid tumor, at 35% many solid tumor, at 5% diffusely amasses a liver. On a lobe follicular lymphomas is only 4% of PELL. The forecast at PELL is bad.

Diagnostic criteria are not defined now.

In Russian Academies of Medical Science from 1944 pts with primary tumor of liver have been treated with PELL. Bopies of tumour of liver in our research it was made by all pts. All diagnoses PELL confirmed by histological and immunohistochemical research of tumor. The age median was 51 years. Men there were 14 women 2, DLBCL were at 14 lymphomas and follicular lymphomas were at 2 pts. The solid lesion of a liver was at 13 patients, and one diffuse. One solid tumor was at 6 of 15 pts. The HCV was 9 pts, HBV - at 2 pts. Serum level HCV RNA and HBV DNA was very high. Median serum level HCV RNA consist 6.810⁶ copies/mL. AFP at all pts was increased from 10 to 50, median 20, CEA was normal at all, and LDG increased at all and fluctuated from 5 to 20 norms. Level ALT and AST was increased from 3 to 35 norms. At pts with hepatitis level ALT and AST was authentically above. At patients without a virus hepatitis of AST was above than at patients, with HCV/HBV ALT was above AST. In bunch of pts with hepatocellular carcinoma (HCC) the age median has composed 65 years. HCV has been tapped at 36 pts, at 52 - HBV, from them at 18 was hepatitis B and at 18 hepatitis C. HCV was at 15 patients, and one diffusive. One solid tumor was at 6 of 15 pts. AFP increased at all pts and fluctuated from 31 to 6600 UI -median 21000 UI. CEA also has been increased and fluctuated from 3 to 20 norms. Level LDG has been increased at 81 patients. Median of LDG was 1.5 norms. In all cases PELL at R-tomograph with contrast tumor of all pts with PELL was pigmentation.

To pts with PELL chemotherapy CHOP. 9 pts R-CHOP 6-pts. 1 pts resorption of a liver was made. Complete remissions have been reached only at 3 pts, partial remissions - at 10 pts, 3 pts - without effect. The median without recurrent survival time was 18 months.

In our research we can conclusion that pts with PELL have high level of LDG, normal level of AFP and CEA, in R-tomograph with contrast PELL all pigopetony.

469 CLINICAL AND MORPHOLOGICAL CHARACTERISTICS OF PRIMARY NON-HODGKIN’S OF PAROTID GLAND LYMPHOMA ASSOCIATED WITH SOJŒGRÈN’S SYNDROME (ONE RUSSIAN CENTER EXPERIENCE)

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Primary parotid gland lymphoma is a rare disease (2.5-7% of all extranodal NHL). The aim of our study were examination of clinical and histopathological characteristics of this type lymphoma associated with SojŒgrÈn’s syndrome.

Materials and methods: In CRC of RAMS since 1983 to 2007^ 44 patients (6,2%) were affected by lymphoma of parotid gland. Diagnosis was proved by immunohistochemical method investigation of tumor.

Results: Median of follow up was 59 months. Female/male ratio: 29/10. Age ranged from 15 to 83 years (the median - 51 year). 26 patients (66,7%) were younger 60 age. The median age of patients was 68 years (range 48–82). Gastralgia and anemia were common symptoms at initial presentation. All patients except 1 received 6 cycles of R-CHOP treatment without consolidation radiation therapy or prior surgery. All patients achieved complete remission, and the estimated overall survival with a median follow-up of 46 months (range 7–92) was 100% without relapse or significant GI adverse effects such as perforation or bleeding during R-CHOP treatment. No long term adverse effects of rituximab were recorded during the observation period. Helicobacter pylori infection was diagnosed in 78.5% of patients, but was eradicated in a limited number of patients.

Conclusions: Our results illustrate the feasibility and effectiveness of the addition of rituximab to conventional CHOP therapy in the management of localized PG-DLCL.

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association Sjogren’s syndrome and lymphoma: complete remission consists 25% vs 52% when this syndrome was not found; early recurrent of disease was in 3 of 4 patients (75%) from 1 to 5 months (2 of there dissemination recurrent) and early death - 3 cases.

Conclusion: preliminary data confirm that association Sjogren’s syndrome and lymphoma has poor prognosis and it is necessary more investigation.

470 RAPIDLY EXPANDING NECK MASS: CONSIDER THYROID LYMPHOMA!

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Background: Thyroid lymphoma is a rare clinical entity accounting for 0.2% of thyroid cancers in Ireland. It commonly presents with a rapidly enlarging neck mass. The aim of this study was to review our experience of thyroid involvement by lymphoma.

Methods: A retrospective review of lymphoma referrals over a 12 year period (1998-2010), identified 12 cases of thyroid involvement. Patient demographics, clinical presentation, investigations, staging, diagnosis, treatment, and outcomes were assessed.

Results: Of the 12 patients, 11 were female. The median age was 69 years (range 22-82 years). Forty six percent presented with a symptomatic neck mass. Median duration of symptoms at presentation was 2 months. Thyroid dysfunction was seen in 75% of patients. On histological review, 9 patients had diffuse large B cell lymphoma, 2 had follicular lymphoma, and 1 had Hodgkin’s lymphoma. Eight of 12 patients presented with stage I/II disease. Seventy five percent of patients were treated with systemic chemotherapy and 25% received a combination of chemotherapy and radiotherapy. A complete response was seen in 8 (67%) patients and a partial response in 2 (17%) patients. Two patients are currently on treatment. Two (17%) patients underwent emergency surgery. The median overall survival was 37 months (6-149 months).

Conclusions: The differential for a rapidly enlarging neck mass includes thyroid lymphoma and anaplastic thyroid cancer, early diagnosis is essential to facilitate appropriate treatment. Successful outcomes may be achieved in patients with thyroid lymphoma.