Non-Hodgkin lymphoma - Clinical

B1601

DIAGNOSTIC SIGNIFICANCE OF PRETREATMENT SERUM LEVEL OF OSTEOPONTIN AND MACROPHAGE CHEMOTACTIC PROTEIN-1 IN PATIENTS WITH DIFFUSE LARGE B CELL LYMPHOMA

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Background: Diffuse large B cell lymphomas (DLBCL) are heterogeneous diseases which vary in biological expression and clinical course. While standard clinical prognostic factors predict outcome in DLBCL, predicting the outcome of patients might be further refined using biological factors. Some biological factors play a role in stimulation of malignant growth, metastasis and angiogenesis; however, their clinical relevance has not yet been well established for most of them.
Aims: The focus of this study was to determine pretreatment serum level of osteopontin (OPN) and macrophage chemotactic protein-1 (MCP-1) in patients with diffuse large B cell lymphoma and to investigate whether these factors provide prognostic information.
Methods: We measured pretreatment serum levels of OPN and MCP-1 by Enzyme-Linked Immunosorbent Assay (ELISA) in 67 patients newly diagnosed as diffuse large B-cell lymphoma and in 30 healthy controls. All patients were treated with rituximab-CHOP chemotherapy.
Results: The serum OPN levels were found elevated in untreated DLBCL patients compared to controls: in patients ranged from 25 to 238 pg/ml; median 94.2 pg/ml while OPN levels of the healthy controls ranged from 13 to 46.5 pg/ml; median 30.0 pg/ml (P=0.00008). There were significant differences in the serum MCP-1 levels between DLBCL patients and controls (median 1395.14 pg/ml vs. 779.3 pg/ml, P=0.035). Serum OPN levels higher than the median level was related to advanced Ann Arbor stage (P=0.026), International Prognostic Index of 2 or higher (P=0.005), ECOG ≥2 (P=0.004). The complete remission rate after treatment was higher in patients with low OPN serum levels than in those with high OPN serum levels (67.5% versus 32.4%, P=0.002). Elevated serum levels of OPN were strongly associated with shorter overall survival (P=0.007) and event-free survival (P=0.04). In multivariate analysis with International Prognostic Index criteria, OPN remained a significant predictor for overall survival (P=0.043). MCP-1 level was significantly correlated with age (P=0.005) and serum lactate dehydrogenase level (P=0.046), bat were not strongly correlated with other potential prognostic factors and it failed to show prognostic significance. A more advanced disease and/or poor prognostic factors were seen in patients who had both serum OPN and MCP-1 levels higher than the median level of the patients.
Summary / Conclusion: Our results showed that pretreatment serum level of OPN is significantly related to outcome in DLBCL patients.

B1602

THE USE OF PET-CT IN THE DIAGNOSIS OF ADULT T CELL LEUKAEMIA – LYMPHOMA SUBTYPES

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Background: The treatment of adult T-cell leukemia lymphoma (ATLL) is poor with median survival rarely exceeding 10 months in the aggressive subtypes. The diagnostic sub categorisation of the disease is important prognostically according to the original classification proposed by Shimoyama, which comprises acute (leukaemic), lymphomatous, smouldering and chronic subtypes. Acute and lymphomatous ATLL constitute the aggressive types and convey a worse prognosis. The role of PET-CT has been extensively investigated in the context of both Hodgkin's and Non-Hodgkin's lymphoma. However, to date no publications have characterised the appearances of the discrete ATLL subtypes on PET-CT.
Aims: Our aim was to characterise the appearances of ATLL subtypes on PET-CT, with particular emphasis on distinguishing aggressive disease from the indolent forms. In addition, we wished to investigate whether a correlation existed between the degree of marrow involvement and 18F-fluoro-deoxyglucose (FDG) uptake on PET-CT.
Methods: We retrospectively analysed 21 cases of ATLL treated at our institutions diagnosed between 2001–2012. 17 of these patients had PET-CT scanning performed as part of their initial diagnostic investigations and 4 after treatment or at progression. Bone marrow samples were described according to degree of disease involvement and correlated to intensity of FDG uptake on PET-CT. Clinical outcomes were correlated to PET-CT and bone marrow findings.
Results: The median age of patients was 49 years (male =9, female =12). 3/21 (14.3%) were categorized as aggressive acute subtype, 12/21 (57.1%) lymphomatous, 3/21 (14.3%) smouldering and 3/21 (14.3%) chronic. The median overall survival for all subtypes was 20.9 months (range 1.3-73.4 months). 16/21 (76.2%) of the patients have died. Patients with intense uptake on PET-CT at baseline (11/17, mean SUVmax 29.6, range SUVmax 9.6-85.2) displayed a tendency to markedly shortened median survival of 10.5 months compared to those with minimal/no uptake (5/17, mean SUV max 2.2, range SUV max 0-3.06) of 24.6 months regardless of subtype, although this was not statistically significant with our number of patients (P=0.28). All lymphomatous cases (n=10) demonstrated evidence of intense FDG avidity at baseline (mean SUVmax 24.5, range SUVmax 9.6-41.0) except 1 patient with no FDG avid disease who had a solitary lesion excised. All 3 cases of smouldering disease had either low or no FDG uptake (mean SUV max 2.0, range SUV max 0-2.88), no evidence of bone marrow involvement and remain alive and well. In 2 cases with excision of a solitary lesion, no uptake was demonstrated elsewhere. Of 19 assessable patients, 7 had documented marrow involvement: 3 had <5% disease bulk of which 1 had FDG uptake in bone. The 2 patients with high bone marrow involvement of 40% and 85-90% respectively both demonstrated intense skeletal FDG avid uptake (mean SUV 15.9).
Summary / Conclusion: In this series, patients with lymphomatous aggressive ATLL all demonstrated intense FDG avid uptake. All cases of smouldering subtype demonstrated minimal FDG uptake. In patients with resected localised skin disease and no evidence of FDG uptake, observation with serial HTLV-1 viral loads may identify those patients at high risk of progression to a more aggressive phenotype. The number of patients with marrow involvement was small, and intense FDG uptake appears to have been associated with greater disease bulk and more aggressive subtypes. Overall this retrospective analysis suggests PET-CT is useful in the diagnostic subclassification, and potentially prognosis of ATLL.

B1603

THE IMPACT OF FCΓ RECEPTOR POLYMORPHISMS AND GLUTATHIONE-S- TRANSFERASES POLYMORPHISMS IN PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA TREATED WITH R-CHOP

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Background: FcγRIIIa polymorphisms have been associated with response to single-agent rituximab in patients with follicular lymphoma and Wandelstrom macroglobulinemia but data regarding DLBCL and follicular lymphoma patients treated with R-CHOP are conflicting. Glutathione transferases (GSTs) polymorphisms have been associated both with favorable and unfavorable outcomes in a variety of cancer types. In Korean DLBCL patients they have been associated with chemotherapy related toxicities.
Aims: In the present study, we evaluated the prognostic impact of polymorphisms of the FcγRIIIa, GSTT1, GSTM1 and GSTP1 genes on the outcome of patients with DLBCL treated with R-CHOP.
Methods: DNA was isolated from peripheral blood or bone marrow samples of 109 patients. The 158V/F polymorphism of the FcγRIIIa gene and the deletions of GSTT1 and GSTM1 were analyzed using multiplex PCR techniques. The Ile^{105}Val polymorphism of the GSTP1 gene was analyzed using a PCR-RFLP technique. PCR products were evaluated on ethidium bromide-stained agarose gels.
Results: Of the 109 patients tested for the FcγRIIIa-158V/F polymorphism, 28 (26%) were carriers of FcγRIIIa-158V/V, 23 (21%) of F/F and 58 (53%) of V/F. With respect to GST polymorphisms, 45 patients (52%) were GSTM1-null, 22 (25%) were GSTT1-null, 10 patients (11%) were GSTP1-105V/V, 42 (47%) were Ile/Ile and 38 (42%) were heterozygous. Eleven patients (13%) were GSTM1/GSTT1-double null, while 45 (52%) had only one deleted gene and 31 (36%) had no deletions. There were no significant associations between FcγRIIIa or GST genotypes and patients' characteristics. Presence of GSTM1-null genotype was not associated with concomitant presence of GSTT1-null genotype (P=0.85), neither was presence of GSTP1-105V/V associated with concomitant presence of GSTM1/GSTT1-double null genotype (P=0.77). The 5-year EFS was 76% for FcγRIIIa-158V/V, 70% for V/F and 64% for F/F (P=0.68). For the GSTP1-105I/V polymorphism, 5-year EFS was 86% for V/V, 67% for V/I and 74% for I/I (P=0.58). The 5-year EFS was 72% for GSTM1-null patients versus 69% for GSTM1+ (P=0.66) and 77% for GSTT1-null versus 69% for GSTT1+ (P=0.47). Finally, 5-year EFS was 90% for GSTM1/GSTT1-double null patients versus 68% for patients with one deleted gene and 71% for patients with no deletions (P=0.59). Given that patients with GSTP1-105V/V genotype and patients with GSTM1/GSTT1-double null genotype had the highest EFS rates (86±13% and 90±9% respectively), further evaluation showed that presence of either GSTM1/GSTT1-double null genotype or GSTP1-105V/V genotype (19 patients in total), was associated with a marginal improvement in EFS compared to any other genotype (P=0.13).

Summary / Conclusion: Our data indicate that there is no individual effect of GSTs polymorphisms on EFS of DLBCL patients treated with R-CHOP. However, carriage of either GSTP1-105V/V polymorphism or GSTM1/GSTT1-double null genotype is present in 20% of patients and is slightly associated with improved EFS. This finding needs confirmation in a larger group of patients.

B1604

MANTLE CELL LYMPHOMA WITH AN INDOLENT BEHAVIORS

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Background: Mantle cell lymphoma makes up from 3 to 10% of non Hodgkins lymphomas. Median age of presentation is 60 years with male predominance. Morfologically limphocytes are small with a slightly indented nucleus and have a characteristic chromosomal translocation (11;14) (q13;q32). The survival of patients varies from 3 to five years, prognostic factors associated with a poor outcome comprise an increased mitotic index, blastic variant, 12 trisomy, aberrant karyotype, p53 gen mutations and peripheral blood involvement.
Aims: Evaluate Mantle cell lymphoma with indolent behavior in our institution
Methods: We have reviewed all mantle cell lymphomas diagnosed during the last 6 years in our Hospital. We studied 20 patients, 16 of them showed an indolent behaviour similar to B cell chronic lymphoid leukemia in A stage of Binet. We showed the results of these patients
Results: The male/female ratio of the patients was 2 to 4. The median age of our subjects was 72 years (range: 62-84 years) At diagnosis most of the patients had associated comorbidities, the most frecuent was HTA. Two patients suffered autoimmune hemolytic anemia before diagnosis of MCL was made and both of them showed good response to corticotherapy. Perypheral blood involvement was present in all cases , no anemia, and no thrombocytopenia appeared, morfologically limphocytes were small with a slightly indented nucleus coarse chromatine, without nucleoli, in one patient blastic cells were present in blood. Cells expressed strong inmunoglobulin , more often lambda light chain, CD5 and FMC7 while they were negative for CD10 and CD23 antigens. Only 3 patients had supra and infradiafragmatic lymphadenopathies inferior to 2 cms. 5 cases showed moderate splenomegaly . A FISH study in peripherical blood was performed in all patients which confirmed positivity for the translocation (11;14), without any others added abnormalities. None of the patients received treatment because of they were asymtomatic, the median follow up was 3 years, range (2-7 years)
Summary / Conclusion: There is a variant of indolent MCL similar to B cell chronic lymphoid leukemia in that affects peripheral blood without adenopathies. This asymptomatic patients without adenopathies should be treated by therapeutical abstention.
All of them were diagnosed following a inmunophenotype in peripheral blood on finding a lymphocytosis. It is important study prognosis factor of an index type of proliferation and added genetic anomalies to t (11;14) so as take therapeutical decisions

B1605

SIMPLE PROGNOSTIC PARAMETERS IN DLBCL: PRETREATMENT SERUM ALBUMIN LEVEL AS AN INDEPENDENT PREDICTOR FOR EFS AND OS

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Background: The International Prognostic Index (IPI) is a widely used and accepted prognostic model for diffuse large B cell lymphoma (DLBCL). In the rituximab era, R-IPI is used as well. In the last years, several groups looked for additional simple prognostic parameters, not included in the original IPI, i.e. absolute lymphocyte count (ALC), absolute monocyte count (AMC) and absolute neutrophil count (ANC), with diverse results.
Aims: The aim of the present study is to evaluate the prognostic value of these parameters such as, ALC, AMC, ALC/AMC, ANC/ALC, hemoglobin and albumin level at diagnosis in patients with DLBCL and compare with known prognostic models as IPI and R-IPI.
Methods: We retrospectively reviewed data of 166 adult patients with DLBCL who were diagnosed at Rabin Medical Center, Israel, between the years 2004-2008. The mean age was 63.4 years, 43% were male, 62% with stage III/IV, 28% with ECOG performance status 0-2, 59% with elevated LDH level and 85% were initially treated with R-CHOP. The median follow up was 6.6 years (range 3.6-9 year).
Results: The 5 years overall survival (OS) for the entire group was 67.5%; for patients with lower IPI (0-2) – 76% (n=83); and for patients with higher IPI (3-5) – 48.8% (n=80). In univariate analysis, pretreatment hemoglobin and albumin levels had statistically significant effect on EFS and OS. Five years OS was 77.3% in patients with pretreatment albumin >3.5 g/dl, compared with 47.9% in patients with albumin level ≤3.5g/dl (P<0.001). Five years EFS was 68.9% *vs.* 45.8%, respectively (P<0.001). Five years OS was 81.7% in patients with pretreatment hemoglobin >12g/dl, compared with 56.5% in patients with hemoglobin level ≤12g/dl (P=0.003). Five years EFS was 74.6% *vs.* 51.1%, respectively (P=0.002). However, univariate analysis did not identify pretreatment ALC, AMC, ALC/AMC and ANC/ALC as predictors for EFS and OS. Multivariate analysis using Cox regression, included the above parameters as well as IPI/R-IPI, showed that pretreatment albumin level was independent prognostic factor (P=0.001) for EFS and OS and its effect was significant as IPI or R-IPI effect.
Summary / Conclusion: Our data showed that albumin level is a strong prognostic factor for EFS and OS, and its effect is as good as IPI or R-IPI effect.

B1606

MANAGEMENT OF THE HBV REACTIVATION IN ISOLATED HBCAB POSITIVE PATIENTS AFFECTED WITH NON HODGKIN LYMPHOMA

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Background: Occult HBV infection (OBI) is defined by the persistence of HBV in the liver without serum HBsAg and HBVDNA. It represents a life threatening risk if the carrier experiences immunosuppression. An OBI can be present in about 18% of HBcAb+ patients. International guidelines suggest a strict surveillance for ALT and HBV markers in patients undergoing immunosuppressive therapies, in particular monoclonal antibodies. In Non-Hodgkin Lymphoma (NHL), OBI reactivation can occur in 3 to 25%. The real prevalence remains to be established.
Aims: To determine the prevalence of occult HBV reactivation in a large cohort of patients undergone immunosuppressive treatments for NHL and to confirm the association with monoclonal antibodies.
Methods: We analysed 498 NHL patients in a single centre of Southern Italy from 2005 to 2011. We evaluated HBV markers, type and NHL localization, treatment type and HBV reactivation.
Results: Fourty percent was treated with monoclonal antibodies and 60.3% without. Ninety six patients were HBcAb+ and HBsAg-. HBV reactivation occurred exclusively in ten subjects of this subgroup, 5 treated with Rituximab and 5 without. Every patient was treated with Lamivudine. No one experienced liver-related death.
Summary / Conclusion: Our data report a prevalence of OBI reactivation of 10.42% in HBcAb positive patients. This event occurred in 50% of cases in patients treated with no monoclonal antibodies. Each reactivation was treated with Lamivudine. This report enlightens the importance and the cost-effectiveness of a strict surveillance in HBcAb+ HBsAg- patients, in order to detect an occult HBV reactivation, also in NHL patients treated with monoclonal antibodies-free protocols.

B1607

EPIGENETIC MARKERS AS PREDICTORS OF RESPONSE IN YOUNG POOR RISK DIFFUSE LARGE B CELL NON HODGKIN'S LYMPHOMA (DLBCL)

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Background: Young patients with poor risk DLBCL are characterized by truly refractory disease. Dose intensification of the standard combination chemotherapy is one of the methods to improve treatment results. DNA methylation is an important regulator of gene transcription; alteration in DNA methylation is common in development and progression of malignancy
Aims: To evaluate the promoter methylation (PM) of 4 genes: p16, p53, MGMT and GST as effective tools in predicting the outcome and prognosis of young poor risk DLBCL patients treated with CHOEP – 14 regimen
Methods: The study included 51 patients with high and high intermediate risk aaIPI DLBCL patients who were treated with CHOEP – 14 regimen. Promotor methylation of the tested genes was done by specific methylation PCR.
Results: Complete remission (CR) was achieved in 38 patients (74.5%). The CR rate was significantly affected by B-symptoms (P=0.03), extra nodal sites (P=0.03) and dose intensity of myelosuppressive drugs (P=0.001). PM of the studied genes was associated with significantly poor response (P=0.001) for the four tested genes. There was also significant relation between the methylation index and the response rate. The relapse rate was 23.7%. The 3 years DFS was 68.8% and 4 years OS was 96% with only one treatment related mortality. There was significant relation between the DFS and p53 PM as well as with p16 PM (P=0.02 and 0.05 respectively) while this relation was not significant with the other two tested genes. The main reported toxicity was myelosuppression, while non hematologic toxicities were infrequent and regressive
Summary / Conclusion: Hypermethylation of the studied genes correlated with poor response; however more studies are required to validate these findings.

B1608

NEITHER CONSOLIDATION RADIOTHERAPY NOR MAINTENANCE WITH RITUXIMAB OFFER ADVANTAGE TO PATIENTS WITH LARGE B CELL LYMPHOMA TREATED WITH STANDARD THERAPY

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Background: Most patients (pts) with diffuse large B cell Lymphoma (DLBCL) treated with R CHOP achieve complete remission (CR). However, a significant percentage relapses. Different strategies try to decrease relapse. Consolidation with radiotherapy (RT) has played a role in the management of DLBCL, but its utility in the Rituximab era is less known. Although a modest benefit of Maintenance with Rituximab (MR) has been suggested, guidelines do not support its use in DLBCL. We present the results of 105 pts with DLBCL who achieved CR after treatment with R CHOP(Epirubicin 75 mg/m^2 substituted Doxorubicin= R CEOP).
Aims: Assess the potential benefit of consolidation RT or MR to decrease relapse. Four groups of pts were defined: first, pts with no further treatment after R CEOP courses, consolidation with RT comprised the second group, MR formed the third group and a fourth group included pts who received RT and MR.
Methods: Between January 2006 and December 2011 all pts ≥ 18 years in CR were included. Risk factors reviewed: age <60 versus ≥60 years, Eastern Cooperative Oncology Group performance status (ECOG 0-2vs >2), Ann Arbor Stage (I-II vs III-IV), Extranodal Disease (ED), Bulky disease(BD) (≥10 cm), International Prognostic Index (IPI low vs high risk),6 versus 8 courses R CEOP, RT and MR. After CR and R CEOP courses, physicians decided if adjuvant treatment was necessary based on their clinical judgment. Involved field RT was delivered at a total dose of 36 Gy. MR was started 3 to 6 months after the last course of R CEOP and consisted of 2 different schedules: Rituximab 375 mg/m^2 one dose weekly for 2 consecutive weeks every 6 months or Rituximab one single dose every 3 months; both schedules until completing 2 years. Time to relapse was measured from the application of the sixth course of R CEOP to relapse.
Results: Median age was 61 years (18-86). Median follow up of all pts was 24 months (1-72). Fifty seven (54%) pts were ≥60 years (69% of them did not receive adjuvant therapy). Seven (7%) subjects had ECOG >2. Advanced Disease was present in 38 (36%)pts. Fifty one (48.5%) pts showed ED. BD was observed in 50 (48%) pts (54% of them received RT). High risk IPI in 22 (14.6%)pts. Seventy six (72%) pts received 6 courses of R CEOP. Sixty six pts (62.8%) received adjuvant therapy: RT 21 (20%) pts, MR 31 (29.5%)pts and 14 (13.3%)pts received RT plus MT. The differences between groups were an older age for the no adjuvant therapy group (p< 0.05) and BD for the RT group (p< 0.04). In all, 17pts (16.1%) have relapsed at a median time of 9 months (3-54).The group with no therapy had 8 relapses, RT 3 relapses, MR 5 relapses and one relapse occurred in the group with both therapies.The 3-year relapse free survival rates were 79.4%, 85.7%, 83.8% and 92.8% for the no adjuvant therapy, RT, MT, and both therapies groups (p <0.4), respectively. For those relapsing, the risk factors were advanced stage (p < 0.009) and high risk disease (p < 0.008).
Summary / Conclusion: The majority of pts are in CR. Nevertheless, most cases had low risk disease. We did not observe difference between groups. BD is usually an indication for RT. However, near half of the pts with BD did not receive RT, and did not have an increase incidence of relapse. MR did not offer benefit. Advanced and High risk diseases were the only risk factors associated to relapse. Therefore, it seems reasonable not to use any further treatment in low risk disease after standard therapy. Prospective trials with larger number of pts are needed to evaluate RT in the rituximab era.

B1609

PROGNOSTIC RELEVANCE OF BASELINE NEUTROPHILE-TO-LYMPHOCYTE RATIO IN DIFFUSE LARGE B-CELL LYMPHOMA : RESULTS FROM A PROSPECTIVE COHORT STUDY

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Background: The systemic inflammatory response and host immunity has been associated with prognosis of various human cancers. The neutrophile-to-lymphocyte ratio (NLR), representing both inflammatory response and imuune status, has been proposed as a reliable marker to predict clinical outcomes in cancer patients.
Aims: The aim of this study is to determine prognostic significance of baseline NLR in patients with diffuse large B-cell lymphoma (DLBCL).
Methods: Subjects were selected from the Samsung Medical Center Lymphoma Cohort Study (a prospective cohort study registered at www.clinicaltrials.gov as NCT00822731). Survival analysis were performed by Kaplan-Meier methods and the log-rank test. To evaluate the independent prognostic significance of NLR, multivariate Cox regression models were applied. The optimal cutoff value of NLR was decided by using ROC curve analysis.
Results: A total of 334 DLBCL patients receiving R-CHOP chemotherapy were included in this study. A NLR value of 3.1 corresponded to the maximum combined sensitivity and specificity on the ROC curve and the AUC (area under the curve) was 0.635 (95% CI 0.581-0.687, P=0.0009). With a median follow-up of 31.1 months (range, 0.3-55.5), patients with baseline NLR>3.1 (n=125) showed poorer overall survival (OS) (P<0.001) and progression-free survival (PFS) (P<0.001) compared to patients with baseline NLR≤3.1 (n=209). The expected 3-year OS and PFS rates were 63.0% vs 86.1% (P<0.001) and 58.0% vs 77.7% (P<0.001), respectively. In univariate analysis, the following variables were predictive of OS: NLR>3.1 (P<0.001), age older than 60 (P<0.001), ECOG≥2 (P<0.001), stage≥3 (P<0.001), high-intermediate or high IPI risk group (P<0.001), extranodal involvement≥2 (P<0.001), and bone marrow involvement (P=0.001). In multivariate analysis, NLR>3.1 (HR 2.0; 95%CI 1.2-3.4, P=0.009), age older than 60 (HR 3.0; 95%CI 1.8-4.9, P<0.001), ECOG≥2 (HR 1.9; 95%CI 1.1-3.3, P=0.021) retained its statistical significance as independent poor prognostic factors for OS.
Summary / Conclusion: This study suggests that baseline NLR is a simple and significant independent prognostic factor for OS in DLBCL patients treated with R-CHOP chemotherapy. Further studies are anticipated exploring the mechanisms of associations between NLR and clinical outcomes in DLBCL, such as inflammatory transcription factors and cytokines.

B1610

18-FLUORODEOXYGLUCOSE (FDG) OUTPERFORMS 18F-FLUOROTHYMIDINE (FLT) IN IDENTIFYING TRANSFORMATION OF FOLLICULAR LYMPHOMA, IN PARTICULAR THROUGH HETEROGENEITY IN UPTAKE

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Background: Diagnosing transformation of follicular lymphoma (FL) to diffuse large B-cell lymphoma is important, since therapy regimens for FL are not effective in transformed lymphoma. Currently, transformation is probably underdiagnosed as transformation is known to occur focally whereas in general a biopsy is performed randomly. FDG-Positron Emission Tomography (PET), imaging glucose utilization, is known to correlate with proliferation rate. However, FLT might more specifically image proliferation through visualization of thymidine uptake.
Aims: Therefore we performed a prospective study to identify which PET-tracer, FDG or FLT, can be used to distinguish between FL and transformed lymphoma.
Methods: FDG- and FLT-PET scans were performed in 17 patients with FL and 9 patients with biopsy-proven transformed lymphoma. We measured SUVmax (standardized uptake value) of the lymph node with the highest uptake per patient and measured the range of uptake in involved nodes per patient. To reduce partial volume effects only lymph nodes larger than 3cc (measured as the A50 isocontour on the PET scan) were incorporated in the analysis. Scans were made on the Philips Gemini TF PET-CT camera, 1 hour after injection of 185 MBq of FDG or FLT.
Results: The SUVmax was significantly higher in transformed lymphoma as compared to FL for both FDG (median 22.0, range 14.6-42.4 in transformed and 10.9 (5.2-20.4) in FL, P<0.0001) and FLT (median 11.5, range 5.5-16.3 in transformed and 8.0 (3.6-16.6) in FL, P=0.03), however, with considerable overlap. Additionally we determined the range of FDG and FLT uptake in each individual patient. The FDG range was significantly higher in patients with transformed lymphoma versus patients with FL (6.0-37.5 versus 0.03-7.9, P<0.001) allowing discrimination between transformed lymphoma and FL. In contrast, FLT did not discriminate (P=0.07, ROC curve: AUC for FDG 0.967 vs FLT 0.716).
Using ROC curve analysis cut off values could be determined. Using a cut off of 14.5 for FDG SUVmax in the lymph node with the highest uptake, transformation was diagnosed with a sensitivity of 100% and a specificity of 82%. With a cut off of 6 for FDGrange, sensitivity was 100% and specificity 71%. For FLT no cut off values could be determined due to overlap of values. For validation, we analyzed FDG PET scans in 4 additional patients with transformed lymphomas and 5 patients with FL using these cut off values. Moreover, we used the same cut off values for 9 transformed lymphomas and 11 FL from literature (Bodet Millin Haematologica 2008). In these validation sets the 100% sensitivity could only be retained using the cut off of 6 for FDG range. The lower specificity found in the validation set (55-80%) is acceptable since it only leads to excess biopsies (when a FL is misclassified as a transformed lymphoma) and not to mistreatment of a patient (when a transformation is missed).
Summary / Conclusion: FDG-PET distinguishes better than FLT-PET between FL and transformed lymphoma. An intraindividual FDGrange of 6 or higher is highly suspicious of transformation and should guide diagnostic procedures.

B1611

FIRST-LINE THERAPY COMBINATION WITH RITUXIMAB AND FLUDARABINE IN PATIENTS WITH EXTRANODAL MARGINAL ZONE B-CELL LYMPHOMA OF THE MUCOSA-ASSOCIATED LYMPHOID TISSUE TYPE.

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Background: There are no consensus guidelines regarding the best therapeutic option for patients for patients with extranodal marginal zone lymphomas of the mucosa-associated lymphoid tissue (MALT) type.
Aims: To evaluate the efficacy and safety of combination first-line therapy with Rituximab plus Fludarabine in extranodal MALT lymphoma patients.
Methods: Patients with untreated or de novo extranodal MALT lymphoma received a combination of rituximab (375 mg/m2 iv) on Day 1 and fludarabine (25 mg/m2 iv) on days 1 to 5 (patients aged > 70 years days 1-3), every 4 weeks. After 3 cycles a work-up was done: those patients who achieved complete remission (CR) received an additional cycle and those in partial remission (PR) received three more cycles.
Results: Twenty-seven patients were included. The median age was 60 years (32-83 y) and 15 (56%) were women. Twelve had gastric MALT lymphoma and 15 extragastric MALT lymphoma. Nine patients (33%) had stage IV disease. After 3 cycles, 16 (59%) of the patients were in RC and 10 (37%) were in PR (1 patient was not evaluated). Thirteen (48%) patients received a total of 4 cycles, 11 (41%) 6 cycles and 3 (11%) 3 cycles. At the end of treatment, 23 (89%) of the patients were in CR and 3 (11%) in PR. With a median follow-up of 66 months, 20 patients (74%) are in CR and 4 (15%) in PR. One patient died due to another malignancy and in two patients we lost follow-up. Toxicities were mild and mostly hematological.
Summary / Conclusion: First-line therapy with Rituximab and Fludarabine is a very active treatment, with a favorable safety profile and long lasting responses for patients with extranodal MALT lymphomas.

B1612

RITUXIMAB, CYTARABINE AND PLATINUM-BASED SALVAGE REGIMEN FOR RELAPSED OR REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMAS (DLBCL): A SINGLE RETROSPECTIVE SURVEY OF 66 PATIENTS

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Background: Addition of Rituximab to CHOP-like first-line chemotherapy regimen has dramatically improved the outcome of DLBCL. Approximately 33% of patients (pts) experience relapse or refractory disease and underneed salvage therapy including high-dose therapy and autologous stem-cell transplantation (ASCT). However the best pre-transplant salvage regimen still remains to be determined (*Gisselbrecht C., CORAL study, J.C.O, 2010*).
Aims: The aim of this retrospective study is to evaluate the response rate after Rituximab, Cytarabine and Platinum-based salvage therapy in relapsed or refractory DLBCL before ASCT.
Methods: Sixty-six pts with refractory or relapsed de-novo DLBCL (n=52) or transformed indolent lymphoma (n=14) are reviewed between 12/2006 and 11/2012. All patients except 1 receive Rituximab in first or subsequent line treatments and all receive salvage regimen based on Rituximab 375 mg/m² d1 i.v., Dexamethasone 40mg/d d1-4 p.o., Cytarabine 2g/m² d2-3 i.v., with either Cisplatinum 100mg/m² d1 i.v.(n=22; 33%) or Carboplatinum AUC 5 d1 i.v. (n=44; 67%). Tumor response is assessed after 3 or 4 cycles by CT-scan (n=4; 6%), PETscan (n=60; 91%) or clinical assessment (n=2; 3%). When it is feasible, pts with CR or PR undergo BEAM conditioning regimen followed by ASCT.
Results: Relapse after first-line therapy occures in 16 pts with a median time of 18 months (7-76). In 50 pts, disease is considered as refractory based on positive PETscan (Deauville criteria) at intermediate assessment after 4 cycles of RCHOP-like regimen (n=43; 86%) or after the end of the front-line therapy (n=7; 14%). Median age is 57 years (23-73). Salvage therapy is administered for 2 (n=11; 17%), 3 (n=48; 73%) or 4 cycles (n=7; 11%) before assessment. The ORR is 74% with 41% CR, 33% PR,6,1% SD and 19,7% PD. Among the responding pts (n=49; 74%), 43 pts (88%) receive BEAM conditioning followed by ASCT. Six pts (12%) are not transplanted because of age (n=4), comorbidity (n=1), active infection (n=1). After a median FU of 13mo (3-65), over the 66 pts, 49 pts (74%) are alive, in CR (n=40; 61%) or in PR (n=3; 5%), 13 pts (20%) died from progressive disease. Among the whole cohort, 5y-OS is 67% without median reached. Among pts in ORR, 1y- and 3y-DFS are 86% and 78% respectively.
Summary / Conclusion: Rituximab-Cytarabine and Platinum-based salvage therapy shows an impressive response rate in relapsed or refractory DLBCL. Although retrospective date, our results compare favourably with published results.

B1613

CELL PROLIFERATION (KI-67) AND BCL2 AS PROGNOSTIC MARKERS IN PERIPHERAL T-CELL LYMPHOMA

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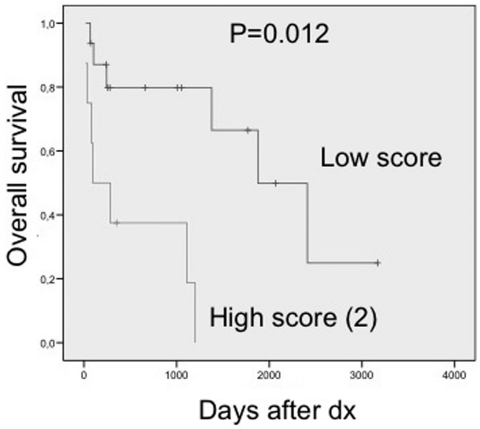
Background: Peripheral T cell lymphomas (PTCL) comprise a heterogeneous group of rare malignancies, characterized by an aggresive clinical course and a poor survival. Although the International Prognostic Index (IPI) and the PTCL prognostic index (PIT) are used for prognostic stratification, their predictive utility is in need of improvement. Proliferation index and chemokine expression may have prognostic significance.
Aims: To investigate the prognostic value of proliferation index (as determined by Ki-67) and BCL2 protein expression (assessed by immunohistochemical methods) in a retrospective cohort of pts with PTCL.



Methods: 37 PTCL cases (28 male, 9 female; median age, 58 year [range, 28-81]) diagnosed between the years 2002 and 2012 were identified. Histology subtypes were as follows: PTCL-not otherwise specified (18, 49%), anaplastic large cell lymphoma-primary systemic type (9, 24%), angioimmunoblastic T-cell lymphoma (7, 19%), T/NK nasal type (2, 5%), intestinal T-cell lymphoma (1, 3%). Proliferation index and bcl-2 expression were reviewed by local hematopathologist. Clinical data was obtained thorough chart review.
Results: Most patients had advanced stage disease, 92% were stage III-IV (Ann-Arbor). 69% had elevated IPI score (3-4-5), and 84% elevated PIT score (2-3-4). The majority of patients (35) received initial treatment with CHOP-like regimens. For the whole group with a median follow-up of 43 months (range 2-139), the median OS was 12.7 months (95% CI, 0-42.1). The median proliferation rate (Ki-67) for the entire group was 80% (range, 10 - 91%; interquantile range, 66 - 80%). Pts with high Ki-67 (>= 80%) at diagnosis (n=21) had a worse OS (median 9.5 months) compared to those with Ki-67 <80% (80.3 months). This difference showed statistical significance (P=0.04) and the Hazard ratio (HR) for Ki-67 >= 80% was 2.7. We found no significant correlation between IPI or PIT scores and Ki-67. By histologic type, angioimmunoblastic T-cell lymphoma showed lower Ki-67 than all other types (55% vs 80%; P=0.013) and this subgroup had better outcome. BCL-2 expression was detected in 76% of the cohort, and showed negative impact on survival (P=0.015; HR=2.347).
We incorporated these variables into a scoring system: 1) a Ki67 index >= 80%, 2) BCL-2 expression. Patients were stratified into two risk groups: low (0 or 1 risk factor) and high risk (2 risk factors). Patients with a high score (2) had: less OS, when compared to the low-risk population (P=0.012) (fig. 1).
Summary / Conclusion: Ki-67>=80% and BCL-2 expression have a negative impact in survival in pts with PTCL, and should be applied in clinical practice.

B1614

AGE DISTRIBUTION OF LYMPHOMA PATHOLOGY SUBTYPES AS PART OF HAEMATOLOGICAL MALIGNANCIES IN JORDAN: A RETROSPECTIVE ANALYSIS OF 2653 CASES IN A TERTIARY CANCER CENTRE.

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Background: Lymphoma is the fourth most common newly diagnosed cancer in Jordan, a small country with a population of 5.85 million.
The age distribution of lymphoma pathology subtypes as a part of the overall haematological malignancies burden in Jordan has not been hitherto well characterized.
Aims: To characterize the clinico-pathological features of lymphoma, and their age distribution, in patients referred to King Hussein Cancer Center (KHCC)(aka Al Amal Cancer centre in the period 1997 to 2003), the major cancer tertiary referral centre in Jordan.
Methods: A retrospective analysis was conducted of all lymphoma patients

referred to KHCC/Al Amal Centre, between 1/6/1997 and 31/1/2012. Clinical features and histological subtypes were retrospectively collected for all patients with a diagnosis of lymphoma, and incorporated in the Lymphoma Service Database

Results: Over the 15 year period of 1997-2012, 5153 patients with haematological malignancies were referred to KHCC/Al Amal Centre . Of those, 2653(51%) had a diagnosis of lymphoma, and thus were registered in the Lymphoma Service Database, of whom 160 (3%) were diagnosed with SLL/CLL and were included in the lymphoma cohort for the purpose of this analysis. 3219 of the cases above(62%) were aged 18 or older. 1692 patients (38%)younger than 18 years of age were classified as pediatric cases. 1150 of the latter group had a diagnosis of leukemia(53% of leukemia cases). On the other hand, 542 pediatric patients were diagnosed with lymphoma, constituting 20% of the lymphoma cases. There were 1074 cases (21% if all cases) of Hodgkin Lymphoma. B-cell lymphomas formed 1310 (87.3%) of the NHLs, whereas T-cell lymphomas formed (104)12.7% of the NHL total. Diffuse large B-cell lymphoma was the most common subtype, with 510 cases (50.7% of all NHLs). Follicular centre-cell lymphomas, B-cell small lymphocytic lymphoma, mantle-cell lymphoma, marginal zone B-cell lymphomas (including MALT lymphomas), and Burkitt lymphoma amounted to 90 (6.4%), 160(11.3%), 14(1.0%), and 43 (3.0%) and12(0.9%) respectively. Among the T-cell lymphomas, mycosis fungoides and anaplastic large-cell lymphomas of T/null-cell type accounted for 31(2.1%) and 27(1.9%) of all NHL cases, respectively.

Summary / Conclusion: To our knowledge, this is the biggest lymphoma series to be reported in Jordan to date. Non-Hodgkin lymphoma appears to constitute a smaller share of the lymphoma burden in Jordan in contrast to Hodgkin Lymphoma, as opposed to Europe and the US, with nearly one third of the cases being classified as Hodgkin Lymphoma. T cell lymphomas constitute a smaller proportion of NHL as opposed to other reports from Eastern Asia, Lymphoma constituted the vast majority of haemtological malignancies in adults, with HD (21%of all cases) and DLBCL (9.9%of all cases) accounting for roughly two thirds of all adult cases. ALL/LL, as expected, accounted for the majority of the haematological malignancies in the pediatric age group The lymphoma clinico-pathological features, however, show important differences from those described in the rest of the world. Follicular lymphoma and mantle-cell lymphoma are less common in Jordan compared to Europe and the USA. Peripheral T-cell lymphomas and T/NK-cell lymphomas of nodal and extranodal nasal types, which are common in other Asian countries, are also less prevalent. DLBCL, as a result, formed a bigger proportion of NHL in Jordan. As described above, HD formed a bigger proportion of haematological malignancies in general, and lymphomas in particular, in Jordan.

B1615

MUM1/IRF4 /BCL6 EXPRESSION FAILS TO PREDICT SURVIVAL IN PATIENTS WITH GERMINAL CENTER B LYMPHOMA TREATED WITH IMUNOCHEMOTHEARPY-SINGLE CENTAR EXPERIENCE

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Background: Diffuse large B-cell lymphoma is subclassifed into molecular subgroups that correspond to different stages of lymphocyte development-namely germinal center B-cell like and activated B-cell like. Myeloma associated oncogene MUM1/ IRF4 is a hallmark of activated B cell lymphoma (ACB). But MUM1 is also expressed in the nucleus or cytoplasm of small percentage of germinal center (GC) B cells located in the “light zone . Unlike normal GC B cells, lymphoma cells in approximately 50% of MUM1 (+) DLCL-B co expressed MUM1 and BCL6.

Aims: In line that MUM1 is predictor of inferior survival the aim of this study was to evaluate MUM1/IRF4/BCL6 immunohistochemical approaches for predicting the survival of patients with GCB lymphoma treated with imunochemotherapy

Methods: Our study enrolled 84 patients diagnosed and treated at the University Clinic of Hematology in the period between January 2002 and January 2012. They were all treated with R-CHOP regimen and the median follow-up of the patient was 36 months. We analyzed biopsy simples immunochemically for markers of germinal center(BCL6), postgerminal center(MUM1), and apoptosis marker (BCL2).

Results: The patients were divided in two groups BCL6+/MUM1+ (39pts;46,4%)and BCL6+/MUM1-(45pts;53,5%). The median overall survival time(OS) were 122,4 months in BCL6+/MUM1-group, and 90 months in BCL6+/MUM1+group respectively. The groups were statistically comparable regarding the prognostic parameters as IPI, performance status.

Summary / Conclusion: Our results did not show any statistical survival advantage and better outcome for the patient classified as GCB DLBL(BCL6/MUM1-) when treated with R-CHOP and indicate that immunohistohemical markers do not really reflect the molecular diversity of the tumor. They also support the studies that suggests that Rituximab eliminates or modulates the significance of some already established prognostic markers for DLBL and indicate that previously recognized markers should be re-evaluated in the context of the modern therapy and that new prognostic indicators for DLBL has to be identified.

B1616

THE USE OF FLIPI AND FLIPI 2 IN FOLLICULAR LYMPHOMA

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Background: Is has been proposed the use of two different prognostic scores when staging Follicular Lymphoma. FLIPI (Follicular Lymphoma International Prognostic Index) is a prognosis index developed in the pre-rituximab era and divides patients into different overall survival (OS) risk groups. FLIPI 2 was developed in the post-rituximab era and is prognostic for progression free survival (PFS).

Aims: To evaluate FLIPI and FLIPI 2 prognostic value.

Methods: We analysed retrospectively 106 patients with follicular lymphoma diagnosed (1997-2012) in our hospital.

Results: The median age at diagnosis was 56 years-old [33;85], 54.7% were male and 43.4% were over 60 years. The median follow-up was 43 months [1;175]. 65.1% patients were in advanced stage (III-IV-Ann Arbor staging system) and 19.1% had B symptoms at diagnosis with 60.4% of extranodal sites. Lymphoma grade was classified (WHO) 1)31.6%, 2)50.7% and 3A) 17.7%, 3B grade lymphomas were not included in the analysis. 36.6% had liver/spleen enlargement and 7.6% had serous effusions. Bulky mass (>6cm) was present in 10.7% and 9.7% had >= 5 nodal sites involvement. 80% had hemoglobin <=12g/dl, no patients had leucopenia (<1.0x10^9/L) and 3% had thrombocytopenia (<100x10^9/L), 31.4% and 24.4% had LDH (lactate dehydrogenase)/B-2 microglubulin elevated. FLIPI: low risk: 45.9%, intermediate risk: 38.8% and high risk: 15.3% (98 patients) and FLIPI 2: low risk: 53.4%, intermediate risk: 29.3% and high risk: 17.3% (75 patients). The treatment strategy was grouped: “Watch&Wait” (WW) (33%) and chemotherapy/radiotherapy (67%). The majority of WW were patients with early stage disease (I-II:58,8%; P<0.0001) and 68.8% had low FLIPI risk (P<0.02). Patients treated with chemotherapy/radiotherapy were mainly at advanced stages (III-IV:79.7%; P<0.0001) and 50% had intermediate FLIPI (P<0.02). No significance found in FLIPI 2 between these two. Comparing different variables in FLIPI/FLIPI 2 we found 13.5% with both high B-2 microglubulin and LDH and 29.8% with only one (P<0.01). In advanced stages 72.1% had bone marrow involvement (P<0.0001). No significance found between nodal regions >=5 vs bulky mass. The 5-year OS was 93.8% and PFS was 63.5%. Six patients have died. FLIPI showed significance in OS with 100% (low risk), 89.1% (intermediate risk) and 83.6% (high risk) patients alive after 5 years (P<0.046) and in PFS with 72.9% (low risk), 59.6% (intermediate risk) and 25.9% (high risk) without progression/relapse after 5 years (P<0.035). FLIPI 2 showed no significant differences either in OS or PFS. In FLIPI, only age and hemoglobin had significance in OS 98,1% (< 60years;P<0.05) and 97.1% (hemoglobin <=12 g/dl; P<0.02) and this was also true for PFS using FLIPI 2: 74% (P<0.001) and 75.1% (P<0.0001) respectively.

Summary / Conclusion: Only variables common to FLIPI and FLIPI 2 had significant prognostic value. Surprisingly patients with hemoglobin lower than 12 showed better OS and PFS at 5 years. As expected FLIPI had value in OS but FLIPI 2 did not show significance in PFS. Whether FLIPI or FLIPI 2 should be used to decide treatment in not clear. This study showed that 68.8% WW group had low FLIPI, hence this maybe helpful to determine therapeutic strategy. The group chemotherapy/radiotherapy was mainly at advanced stages with 50% intermediate FLIPI.

B1617

BENDAMUSTINE PLUS RITUXIMAB IN PATIENTS WITH RELAPSED OR REFRACTORY WALDENSTRÖM’S MACROGLOBULINEMIA (WM)

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Background: WM is an incurable disease, with an overall medial survival of only 5-6 years. Age, hemoglobin level, platelet count, β(2) microglobulin, and monoclonal IgM concentrations are characteristics required for prognosis. First-line therapy of WM has been based on single-agent or combination therapy with alkylator agents (e.g. chlorambucil or cyclophasphamide), nucleoside analogues (cladribine or fludarabine), and the monoclonal antibody rituximab.

Aims: Novel therapeutic agents that have demonstrated efficacy in WM include thalidomide, lenalidomide, bortezomib, everolimus and bendamustine.

Methods: We report the treatment outcome for 16 (9 male, 7 female; median age: 70y, range: 67-78) relapsed/refractory Waldenström’s macroglobulinemia (WM) patients. Treatment consisted of bendamustine (90 mg/m(2) I.V. on days2, 3) and rituximab (375 mg/m(2) I.V. on day 1) for all patients. One rituximab-intolerant patient received bendamustine alone. Each cycle was 4 weeks, and median number of treatment cycles was 4.

Results: The clinical stage (remission, progression or stable disease) was defined with clinical re-evaluation after chemotherapy and re-staging 6 months

after end of therapy. At best response, median serum IgM declined from 3500 to 500 mg/dL, and hematocrit rose from 29.9% to 37.8%. Overall response rate (CR + PR) was 81.2%. Overall therapy was well tolerated. Prolonged myelosuppression was more common in patients who received prior nucleoside analogues.
Summary / Conclusion: Bendamustine in combination with Rituximab demonstrates an excellent effectiveness in previously treated WM patients, with an acceptable toxicity profile. These agents, when compared to traditional chemotherapeutic agents, may lead in the future to higher responses, longer remissions and better quality of life for patients with WM.

B1618
ORAL MUCOSA NON-HODGKIN'S LYMPHOMAS: A CLINICOPATHOLOGIC STUDY OF 22 CASES
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Background: Oral non Hodgkin lymphomas (NHL), is a rare subgroup of NHL. Represent less than 5% of the oral cavity malignancies and 2% of all extra-nodal NHL. The vast majority of them is located in the Waldeyer's ring, mostly in tonsils (70%), but they also may affect the salivary glands, the bone of the jaws and the oral mucosa.
Aims: To report the clinical and laboratory characteristics, as well as the outcome of patients with oral mucosa-NHL (OM-NHL).
Methods: We performed a retrospective analysis of 22 patients records, diagnosed with OM-NHL from 1997 until 2012. Patients with Waldeyer's ring lymphoma (including tonsils), salivary gland lymphoma, and lymphomas that affected the bone of the jaws were excluded from this study. Data, related to histological subtype, clinical stage at diagnosis, international prognostic index (IPI), bulky disease, B-symptoms, treatment administered, response rates, 5-year failure free survival (FFS) and overall survival rate (OS), were recorded.
Results: 12 patients were were male and 10 female, with a median age of 58 years. After staging, (An-Arbor System), oral mucosa was the only site of involvement in 73% (Stage-IE), while 18% were clinical stage II and 9% clinical stage IV. The location of NHL was: tongue 45%, gingival mucosa 23%, palate 14%, lips 14% and the mouth floor 4%. A B-cell phenotype was documented in 64% and a T-cell in 36%. The most common histological subtype was found to be diffuse large B cell lymphoma (DLBCL) in 45%, followed by peripheral T-NHL (PTCL-NOS) in 32%. 9% were diagnosed with mantle cell lymphoma (MCL), 9% with follicular lymphoma (FL) and 5% with anaplastic large cell lymphoma (ALCL). Increased levels of LDH were recorded in one patient, bulky disease in 4/22 patients (2 DLBCL, 1FL, 1 MCL pleiomorphic), B-symptoms also in 4/22 patients (1 DLBCL, 1 FL, 1 MCL, 1 MCL pleiomorphic). Treatment included immunochemotherapy (41%), chemotherapy (31%), immunotherapy (23%) and radiotherapy (RT) followed by chemotherapy (5%). 5/9 patients with NHL of T-cell origin were placed on Interferon-α (INF-α) treatment, while 8/13 patients with NHL of B-cell origin received as first line treatment immunochemotherapy R-CHOP. Among the treatment modalities used in the T-NHL group, INF-α, either as monotherapy or as a rescue therapy in relapsing patients, was highly effective, producing long lasting CRs. After a median follow-up of 64 months, the vast majority of our patients (91%) is alive, while 77% of them are in complete remission (CR). We did not record any significant difference in response and survival rates between the two major histological subtypes (B-NHL versus T-NHL).
Summary / Conclusion: This is one of the largest series focusing on NHL exclusively on the oral mucosa. Our results are contributing in the understanding of the clinical behavior of this NHL subgroup. The percentage of OM-NHL originating from T-cells was significantly higher (36.4%) than that reported for the nodal T-NHL. Response rates are remarkably high, with a long lasting overall survival, independently of the histological subtype.

B1619
RETROSPECTIVE REVIEW OF PERIPHERAL T-CELL LYMPHOMA IN A SINGLE INSTITUTION: OUTCOME AND CENTRAL NERVOUS SYSTEM INVOLVEMENT
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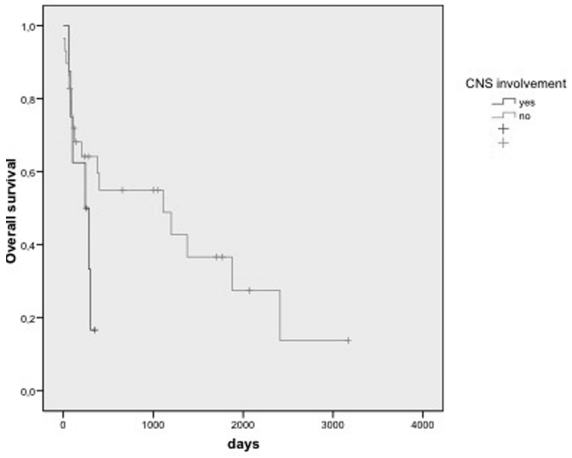
Background: Peripheral T cell lymphomas (PTCL) comprise a heterogeneous group of rare malignancies, characterized by an aggresive clinical course and frequent extranodal involvement. Moreover, little data exist on the risk of central nervous system involvement (CNS) by these lymphomas.
Aims: To describe the clinical characteristics and outcome of PTCL patients, and to estimate the frequency of CNS involvement.
Methods: Retrospective analysis of all PTCL cases diagnosed in Gijon (Asturias, Spain), that covers a population of approximately 450,000 people, between 2002 and 2012. Clinical data were obtained thorough chart review. CNS involvement was defined by positive finding in citology or flow cytometry analysis of CSF.
Results: A total of 37 cases were identified, the histology subtypes were: PTCL-not otherwise specified (18, 49%), anaplastic large cell lymphoma-primary systemic type (9, 24%), angioimmunoblastic T-cell lymphoma (7, 19%), T/NK nasal type (2, 5%), intestinal T-cell lymphoma (1, 3%). 3 patients had received another diagnosis (B-cell lymphoma, Hodgkin's disease) prior to the current diagnosis of PTCL. One case was diagnosed post-mortem. Median age at time of presentation was 58 (range 28-81) years, 35% were ≥65 years old. ECOG was 2-4 in 57%, and 68% had B symptoms. Most patients had advanced stage disease: 92% were stage III-IV (Ann-Arbor), 76% had extranodal involvement, and 38% had documented bone marrow involvement. 69% had elevated IPI score (3-5), and 84% elevated PIT score (2-4). Laboratory data showed elevated LDH level in 73% and elevated Beta-2-microglobulin in 76%. A total of 35 pts received initial treatment, the majority received CHOP-like regimens. 8 pts (22%) received consolidation with autologous stem cell transplant (ASCT) in 1st remission. At the end of first line therapy, overall response was 57% (17 pts CR; 4 pts PR), while 7 cases (19%) had disease progression and 22% experienced early death during treatment. Overall, 19 pts (51%) presented relapse/progression: 15 were treated with platinum-containin regimens, and 5 pts underwent salvage SCT (4 allogeneic, 1 autologous). With a median follow-up of 1298 days (range 79-4173), the median OS for the whole group was 382 days (95% CI, 0-1262). Pts who received transplant in 1st remission had better outcomes than as salvage treatment (P=0.029). CNS disease, as detected by flow cytometry, was found in 8 pts (22%), with no case found in angioimmunoblastic subtype and the highest number of cases in ALCL (4 cases, 50%), and NOS (3 cases, 37.5%). Median time to CNS involvement was 67.5 days (range, 33-296), and univariate analysis only identified elevated LDH (P=0.05) as risk factor for CNS disease, without correlation with BM involvement. Median OS for this group of pts was particularly dismal (244 days, CI 29 - 459 days) (fig. 1).
Summary / Conclusion: This 10-year review of patients treated in a single institution confirms the poor clinical outcomes of PTCL: advanced stage, extranodal involvement, high rate of early death, poor response to front-line treatment, and short OS after relapse. We also find a strikingly high frequency of CNS involvement, as detected by flow cytometry. A CNS surveillance and prophylaxis strategy should be considered for this type of lymphomas.



B1620
IMPACT ON SURVIVAL ACCORDING TO HISTOLOGICAL GRADE (1-2 VS 3A) IN A SERIES OF 128 PATIENTS DIAGNOSED OF FOLLICULAR LYMPHOMA IN THE RITUXIMAB ERA. EXPERIENCE IN ICO-HOSPITAL DURAN I REYNALS.
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Background: Around 15-25% of all follicular lymphoma (FL) are histological grade 3a and comparing with grade 1-2 have different clinicobiological features.
Aims: To analyze clinicobiological characteristics, response to therapy and outcome of a series of 128 patients according to histological grade 1-2 vs 3a in a single institution.
Methods: Between 2004 to 2012 were identified in our data base among 128

patients diagnosed with follicular lymphoma. Histological grades were: grade 1-2, 91 patients (71%); grade 3a, 30 patients (23%) and grade 3b, 7 patients (6%). Histological grades were reviewed according to WHO criteria. We analyzed the clinical and biological features, response rate and prognosis of 121 patients with histological grades 1-2 and 3a.

	FL grade 1-2 (N=91)	FL grade 3a (N=30)	P
Watch and Wait	6/91	0/30	NS
1st line Chemotherapy (N)	91	30	
R-CHOP/R-COP like (%)	82 (90)	30 (100)	NS
R plus Fludarabine analogues (%)	6 (7)	0 (0)	NS
Monotherapy with rituximab(%)	3 (3)	0 (0)	NS
Complementary Radiotherapy	1 (1)	4 (13)	0.04
CR and CRu (%)	59/89* (66)	26/30 (90)	**0.015**
OS at 5 years (%)	81	73	0.39
EFS at 5 years (%)	58	43	0.4
CD10 (%)	93	82	0.12
Bcl2 (%)	95	93	NS
Bcl6 (%)	100	100	NS
Ki-67 > 50% (%)**	17	41	**0.052**

* Two patients not yet evaluated **Performed in 30 and 22 cases, respectively

Results: The clinical characteristics of patients with histologic grade 1-2 vs 3a were: 41M/50F vs 8M/22F; median age, 57 vs 62.5; stage III-IV, 90% vs 77%; B symptoms, 16% vs 10%; high LDH, 31% vs 41% and high β2microglobulina 57% vs 59%, respectively. The percentage of patients with high risk IPI, FLIPI and FLIPI 2 according to grade 1-2 vs 3a was: 6.5% vs 15%, 42% vs 38% and 43.5% vs 45% respectively. Biological data at diagnosis, therapy, response rates, overall survival and event free survival at 5 years are shown in the table. With a not reached median overall survival, 21 (17%) patients died, 14(15,4%) of them with histological grade 1-2 and 7 with histological grade 3a, mostly due to disease progression. Ki-67 index > 50% at diagnosis predict a worse OS at 5 years (54% vs 91%, P=0.072). The probability of transformation to high-grade lymphoma for grade 1-2 vs 3a was 5.5% vs 10% at 5 years (P=0.13), respectively. In multivariate analysis, IPI, FLIPI and FLIPI 2 at diagnosis of all series were the main prognostic factors for survival.
Summary / Conclusion: In our series, histologic grade follicular lymphoma 3a has peculiar biological characteristics, lower expression of CD10 and especially a higher proliferative index. Although patients with histological grade 3a have a significant higher rate of complete remission, OS and EFS are similar in both groups.

B1621
PROGNOSTIC VALUE OF 18 F-FDG TEP IN DLBCL ELDERLY PATIENTS TREATED WITH IMMUNO-CHEMOTHERAPY
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Background: Diffuse large B-cell lymphomas are heterogeneous family of blood diseases which prognosis depends on specific phenotypic, molecular and pathological features. One of the techniques for the evaluation and response is 18 F-FDG PET scanner. If PET scanner imagings at diagnostic (initial extension) and at the end of the treatment (response evaluation) haveal-ready shown their interest through several studies, the impact of the interim evaluation on survival is not yet consensual.
Aims: We conducted a retrospective, monocentric cohort study, to characterize the predictive value of such interim PET scanner (3 courses of treatment) in DLBCL elderly patients treated with R-PMitCEBO.
Methods: We evaluated39 patients aged over 65 years, diagnosed with DLBCL between 2006 and 2011. Patients received immunochemotherapy (R-PMitCEBO regimen) for 6 cycles. Therapeutic response was evaluated according to Cheason 2005 criteria, after 3 and 6 cycles of chemotherapy. An assessment of overall survival (OS) and disease-free survival (DFS) was performed for all patients. Two evaluations were conducted, the first to compare patients in complete remission versus those who are not (CR / nonRC). The second evaluation compares the patients in complete remission versus those in partial remission. (CR / PR).
Results: Among the 39patients, 24 were in complete remission (CR) after 3 courses, 10 in partial remission (PR) and 5 in stable disease (SD). Two year outcome evaluation (CR / notCR at 3 cycles) find PFS at82% for patients with CR and only 29% for patients in nonCR; OS was 78% in formers against 38% among others. More precisely, evaluation of patients with CR compared to PR, provides a two-year PFS was 82% for formers against 50% for laters and a two-year OS of 78% and 50% respectively.
Summary / Conclusion: In elderly patientstreated with R-PMitCEBO, immunochemotherapy for DLBCL, assessment by 18 F-FDG PET scanner is an essential tool for diagnosic and therapeutic monitoring. The interim evaluation after three cycles of chemotherapy has a strong predictive impact on overall survival and disease-free survival for this profile of patients. The use of interim PET scanner allows to rapidly switch the treatment for a another one to maximise the chances to obtain complete remission instead of partial remission or stable disease.

B1622
LANGERHANS CELL HISTIOCYTOSIS IN ADULT PATIENTS: SINGLE INSTITUTION EXPERIENCE
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Background: Objective: Langerhans cell histiocytosis (LCH) is characterized by abnormal proliferation of histiocytes. It is rare disease with an incidance of 1 -2/ million. Although it is more frequent in children at 1-3 years old, it can be diagnosed in all ages. Disease can be presented by multifocal or localized organ infiltrations. Although all systems and organs mıght be infiltrated, main sites for disease is bone, especially skeletal bones. Treatment options differs according to its presentation as local or multifocal. At local disease, only radiotherapy can be effective modality but patients with multifocal disease should be treated with systemic chemothepies or with combination.
Aims: At this study, we aimed to retrospectively analyse our adult LCH patients diagnosed between 1992-2012
Results: Twenty-one patients, 13 male and 8 female, were retrospectively analyzed. Median age was 29(range, 18-53). All of the patients had bone involvement and bone pain has been most prominent complaint according to the involvement site. We documented poliuria and polidipsia in one patient due to hypophysis involvement in addition to bone. 13 (%15 female, %85 male) patients were presented with local disease and 8(%25 male, 75 female) patients had multifocal disease. The characteristics of the patients were given at table 1. The patients with local disease were treated with only radiotherapy and then followed up. The patients with systemic disease were treated with both radiotherapy and chemotherapy. During the treatment period,any grade 3-4 hematological side effects were not documented. The median period of follow-up was 19 (range, 4-120) months. We determined 7 relapses in 4 patients. All of the relapses were detected with bone lesions and they were treated with radiotherapy successfully. Median overall survival was 19 months. 6 patients were lost to follow up. No deaths were recorded during follow up.
Summary / Conclusion: At this retrospective study with relatively limited number of patients, we reported that adult onset LCH patients were mostly presented as a focal disease with bone pain. The radiotherapy was an effective tretatment modality at these patinets. Although, LCH is a rare disease in adult age groups, it should be considered in patients with bone lesions.

B1623
RITUXIMAB MAINTENANCE THERAPY IN DIFFUSE LARGE B-CELL LYMPHOMA: SINGLE CENTER EXPERIENCE
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Background: Diffuse large B cell lymphoma (DLBCL) are curable group of lymphoma with improved outcome mainly due to the incorporation of the anti-CD20 monoclonal antibody, Rituximab (R) to the standard chemotherapy regimens. According to clinical and pharmacokinetic data, prolonged exposure to Rituximab is associated with higher response rates and improved quality of response. Although most of the big clinical studies are not finished, so far, initial findings are not very promising in regard to the overall survival (OS) and progression free survival (PFS) for the patients receiving maintenance treatment in comparison with patients without maintenance treatment after completion of standard therapy with R-CHOP.
Aims: Here, we present our experience with the Rituximab maintenance treatment of DLBCL patients (pts) that were treated at the University Clinic of Hematology in the past 4 years.
Methods: Since 2006, at our Clinic, 42 pts with DLBCL that were not included in a clinical study underwent R maintenance treatment. Pts received Rituximab (375 mg/m^2) every 3 months for 2 years. Our control group consisted of 65 DLBL pts that were treated in same period at our Institution and do not underwent maintenance treatment. Our two groups were comparable regarding the age, gender and IPI score distribution. All evaluated pts initially received 8 cycles of standard R-CHOP regimen. Only pts in complete remission underwent R maintenance treatment. CR was required for entrance in the control group two. We evaluated and compared the progression free survival (PFS), overall survival (OS) between the two groups. Moreover, we evaluated the tolerance of R maintenance treatment and the impact of prolonged R use at pts quality of life (QoL).
Results: After a median follow up of 42 months, PFS was excellent with 32,5% in the treatment group and 27.7 % in the control group. There was no significant statistical difference regarding those two parameters in both groups (P>0.05). Maintenance therapy was generally well tolerated, but we noticed marked and prolonged hypogammaglobulinaemia in the maintenance group. Further investigation of the median initial and follow up serum imunnoglobulin G (IgG) levels in both groups showed : 10,7 g/L and5,07 g/L in the treatment group, respectively, and 13,8 g/L and8,9 g/L in the control group. Statistical correlations of those results showed that maintenance group has statistically significant lower IgG levels (t-test, P<0,05).Furthermore, more frequent hos-

pitalizations and requirement of immunoglobulin therapy were registered in the maintenance group due to the occurrence of recurrent infections, which worsened QoL of those pts.
Summary / Conclusion: In our experience R maintenance therapy did not improve PFS or OS in pts with DLBCL. More over, pts from the maintenance group had a significantly higher risk of developing hypogammaglobulinemia. Our results suggest that risk of developing symptomatic hypogammaglobulinemia should be considered before starting R maintenance. It is in our opinion that evaluation of a larger patient population, together with a longer follow-up is needed before establishing R-maintenance treatment as standard therapeutical approach for DLBL pts..

B1624
CARDIOTOXICITY MONITORING WITH A NOVEL COMBINED APPROACH OF TELEMEDICINE AND BIOMARKERS IN LYMPHOMA PATIENTS TREATED WITH CONVENTIONAL AND LIPOSOMAL ANTHRACYCLINES
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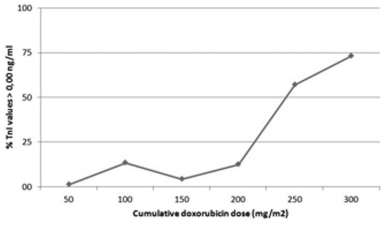
Background: Anthracyclines (AC) are highly effective cytotoxic drugs both in solid and hematological malignancies, whose use, however, is limited by the occurrence of cardiac toxicity (CT). In recent studies intensive cardiac monitoring (with echocardiography *or* biomarkers) has shown to provide an early identification of subclinical cardiac damage: in this case prompt suspension of the AC treatment and aggressive management of the asymptomatic cardiac dysfunction can lead to reversal of the cardiac injury. Liposomal AC formulation has been invoked as a CT-sparing treatment with similar antitumoral activity, especially in old patients or those with cardiac disease.
Aims: Study endpoints are: to measure with the combined monitoring approach the incidence of CT, measured as reduction in the left ventricular ejection fraction (LVEF), rises in TnI levels, significant ECG changes.A telemedicine (TM) system was integrated in this setting to allow for an optimization of health care resources, an increased compliance to intensive monitoring without impacting on the quality of care provided



19 patients	Cumulative doxorubicin dose(mg/m²)					
	50	100	150	200	250	300
TnI controls performed	71	59	45	32	14	15
TnI values > 0,00 ng/ml*	1	8	2	4	8	11
% TnI values > 0,00 ng/ml	1.4	13.6	4.4	12.5	57.1	73.3

Fig.1: Trend for increasing TnI values with increasing cumulative doxorubicin dose

*Only 2 values above 0,08 ng/ml

Methods: This is a prospective observational trial in lymphoma patients undergoing treatment with conventional or liposomal AC. Informed consent was obtained from each enrolled patient. We used a comprehensive approach to monitor for AC CT, using echocardiography, ECG and biomarkers (Troponin I - TnI). Clinical, echo, ECG and TnI data were acquired in our Hematology Clinic and transferred via TM to be evaluated by the reporting cardiologist.
Results: The study enrolled 20 patients, 13 males and 7 females. The median age at diagnosis was 40.9 years (range 20.1 to 78.2 years). 14 patients had a diagnosis of non-Hodgkin's lymphoma and 6 of Hodgkin's lymphoma. Two patients underwent chemotherapy with liposomal AC, all the others with conventional AC. Three patients had at least one cardiovascular risk factor. In six months we performed 216 TM assessments. Compliance to the protocol was excellent as 97.4% of the planned TM evaluations and 94% of the programmed TnI controls, were actually performed. In all cases, the data were successfully transferred to the cardiologist's client. The average time to perform a complete TM assessment was 19 m and 47s, while less than 6 minutes were used for the echocardiographic examination. It took less than 5 minutes on average by the cardiologist to evaluate data from 1 TM assessment and to produce a report. The primary endpoint (reduction in LVEF), did not occur in any of the 19 evaluable patients. In two patients the monitoring detected asymptomatic signs of cardiac ischemia (in one case diffuse T-waves inversion in anterior leads, in the other posterior wall hypocinesia and moderate TnI rise): both patients underwent percutaneous coronary intervention with optimal myocardial revascularization. In both cases patients were aged >65 years and had a cardiovascular risk factor. These cases were not thought to be related to AC. The patients completed the planned chemotherapy course and they are well. In six patients, at some point during the monitoring, a pericardial effusion was found, in all cases not symptomatic. Except the above mentioned case, none of the patients developed a TnI rise above our laboratory cut-off (0.08 ng/ml). However, with increasing cumulative AC doses, we observed a progressive increase in TnI values > 0.00 ng/ml (Figure 1).
Summary / Conclusion: AC CT monitoring is recommended by most guidelines but seldom practiced. Our innovative approach of integrating different detection methods through a TM system allows for a feasible and accurate monitoring of AC CT, and makes possible the application of a preventive strategy for AC CT.

B1625
LOW DOSE BENDAMUSTINE IN LYMPHOPROLIFERATIVE DISEASE: A SINGLE CENTER EXPERIENCE
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Background: Experience with Bendamustine has grown in various hematologic neoplasms both in relapsed/refractory patients and at diagnosis. Results are very encouraging with clinical and long lasting response. Treatment is usually well tolerated also in older and/or unfit patients and in those with renal impairment.
Aims: We report here our observation of low dose bendamustine in a wide group of hematologic patients treated at our Institution.

Table 1	Patient's features		
Diagnosis		Total number	38
Waldestrom disease	3	Male/Female	19/19
DLBCL	3	Median age	67,4 (20-89)
Multiple myeloma	1		
Mantle cell lymphoma	2	Disease status at treatment	12 (3,5%)
Hodgkin disease	3	Diagnosis	5 (13,3%)
Hairy Cell Leukemia	6 (15,8%)	Refractory Patients	21 (55,2%)
Chronic lymphocytic leukemia	7 (18,4%)	Relapsed	
Follicular lymphoma	10 (26,4%)		

Table 2	ORR	PR	CR	NV	NR	PFS	DFS	OS
All patients	73,6 %	39,5 %	34,2 %	7,9 %	18,4 %	54,5 %	46,3 %	77,3 %
Disease status								
Diagnosis	100 %	41, 7 %	58,3 %	-	-	100 %	100 %	100 %
Refractory	60 %	60 %	-	-	40 %	33 %	50 %	53 %
Relapse > 2	44,4 %	44,4 %	-	11,1 %	44,4 %	23 %	66 %	56 %
Relapse < 2	74,9 %	33,3 %	41, 6 %	16,6 %	8,3 %	75 %	37,5 %	100 %
Diagnosis								
HCL	100 %	-	100 %	-	-	100 %	-	100 %
Follicular Lymphoma	80 %	40 %	40 %	10 %	10 %	88 %	-	67 %
CLL	71,4 %	42,8 %	28,6 %	14,6 %	14,3 %	57 %	-	100 %

Methods: We considered a total of 38 patients with different hematologic diagnosis with a median age of 67.4 years (20-89). 36/38 were treated with low dose (50-60 mg/m^2) Bendamustine (days1,2) in association with rituximab 375 mg/m^2 (day 3) with the exclusion of MM and HL cases. Cycles (4 to 8) were repeated every 28 days. Two patients were treated with lower dose due to comorbities. Patients were treated at diagnosis (31.5%), relapse (55.2%) and progression (13.3). Patients and treatment characteristics are summarized in table 1. Response was defined according to Cheson Criteria, toxicities on the basis of CTC criteria. Statistical analysis we utilized Prism software (MacOS).
Results: 36/38 were evaluable. Treatment was well tolerated in the majority of patients. One patient had to stop treatment due to skin lesions, that occurred in 4 patients (10.5%). Infections were noted in 8/36 patients (21.5%) but not clinically relevant. Hematologic toxicities were mild with 4 case of grade IV neutropenia (10.5%). Among the whole group overall response rate (ORR) was 73.6 % with complete (CR) and partial response (PR) respectively of 34.2 % and 39.5 %. Non responders patients were 3/38 (7.9%). We look for response considering diagnosis (CLL, follicular NHL, HCL) and disease status at treatment (diagnosis, progression and relapse). Patients with HCL (n=6) had impressive response with 100 % CR and no relapses, in those with follicular NHL and CLL had ORR of 80% and 71.4 % respectively Patients at diagnosis have an ORR of 100 % (PR 41,7 %, CR 58.3%), refractory patient responded in 60% cases. We split the group of relapsed patients in those who had less or more than two relapses. Patients in 1st o 2nd relapse had a ORR , PR and CR of, 74.9%, 41.6% and 33.3 %, while in those in subsequent relapse ORR were 44,4% with only PRs and 4/9 patient refractory to treatment. OS, DFS and PFS at 15 months for the whole group were respectively 77,3 %, 46,3 %, 54,8%. But when we split PFS in groups we see how patients at diagnosis had a PFS 100 %, in 1st and 2nd relapse of 77 % , while those treated later or in progression of 33 % and 23 %. Response are summarized in table 2.
Summary / Conclusion: Our experience with low dose bendamustine showed a very good safety and tolerance profile also in elderly and unfit patients with

mild infective and hematology toxicities. Responses were satisfactory in the whole group that comprised also multi-treated and refractory patients. Patients at diagnosis and in particular those with hairy cell leukemia had better response with ORR of 100 % and no relapse observed so far. Even those who were treated later in disease history or in progression could be rescued, but often with not long lasting response. In conclusion we confirm the satisfactory data with bendamustine in lymphoproliferative disorders, results that can be obtained also con lower dose and in unfit patients. Results are much better in untreated/low treated patients and with low grade lymphomas, especially in HCL. These observation should be confirmed with longer follow up and more patients.

B1626

HIGHLY ACTION ANTIRETROVIRAL THERAPY (HAART) IMPROVED EFFICIENCY OF CHEMOTHERAPY IN PATIENTS WITH HIV-ASSOCIATED NON-HODGKIN'S LYMPHOMAS (HIV-NHL)

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Background: In total 40 315 patients were diagnosed with HIV infection in Samara region of Russia: 89.8% directly in the town and 11.2% in the surrounding region. 4774 (11.8%) pts died at the time of this analysis. Risk of developing of NHL in these patients was more than 100 times greater than in the general population.
Aims: To analysis of the epidemiology of HIV-NHL, their own experience of their treatment.
Methods:
During2002-2010, 47 patients with NHL-HIV were treated in our center. Three groups of patients were analyzed: (1) 25 received HAART plus CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy (CT) and (2) 15 – only CHOP chemotherapy and 17 only best supportive care. HAART consisted of a combination of three antiretroviral drugs. Response on HAART was defined as increasing the number of CD4+ cells >10x10^6/L and a decrease in viral load <500 copies/ml.
Results: Median of time from diagnosis of HIV infection to NHL development was 3.7 years. Median age pts was 32,5±2,4 years (range, 01-99). Abs (67%) cases were classified as diffuse large B-cell lymphoma (DLBCL), abs (6%) – spleen marginal zone B-cell lymphoma (SMZL), and abs (27%) follicular lymphoma (FL). Abs (47%) patients had a number of CD4+ cells <10x10^6/L at the start of the NHL treatment. The median overall survival (OS) was 18.4 months for the group 1 (HAART plus CT) against 7.5 months (P<0.05) for group 2 (CT) and 4.4 months (P<0.05) for the group 3 (best supportive care). For patients, which therapy was initiated (n=42), unfavorable prognostic factors were age >60 years, AIDS–phase of HIV, Hb <10.0 g/dl, elevated levels of LDH and non-availability of HAART (P<0.05).
Summary / Conclusion: Our data retrospective data suggest that combination of chemotherapy with HAART improved outcome in patients with HIV-NHL. Increasing the number of CD4+ cells and reduction of viral load is essential for the success of chemotherapy.

B1627

THE ROLE OF CONSOLIDATIVE RADIOTHERAPY IN DIFFUSE LARGE B CELL LYMPHOMA PATIENTS WITH BULKY DISEASE.

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Background: Bulky disease, remains to be a significant prognostic factor for non Hodgkin lymphoma patients .The role of consolidative radiotherapy in these patients is still contraversial. Diffuse large B cell lymphoma patients is 30%>40% of all non Hodgkin lymphoma patients.Bulky disease, remains to be a significant prognostic factor for non Hodgkin lymphoma patients .The role of consolidative radiotherapy in these patients is still contraversial.
Aims: So, we aimed to asess the role of radiotherapy in diffuse large B cell lymphoma patients with bulky disease.
Methods: We retrospectively included 92 patients with non hodgkin lymphoma, subtype of diffuse large B cell who had bulky disease in Ankara Oncology Hospital.Bulky disease was defined as the size of lymphadenopathy over 5 cm. Patients characteristics were summarized in Table 1. All patients were treated with six –eight cycles of RCHOP chemotherapy.We excluded patients in whom complete remission with first line chemotherapy could not be achieved and grouped 65 patients in first complete remission in to those treated with radiotherapy(n:22) and not(n:43).We aimed to asess the relapse rates and progression free survival difference between the groups
Results: Median follow up of the patients were 30(6-149) months.Patients in both groups were similar according to age,sex and IPI score. There were statistically significantly higher number of patients with advanced disease status in non radiotherapy group. The number of patients who relapsed during the follow up were not statistically different between the groups. (5/22 vs 10/43 , p:0.962).Although, 4 years progression free survival was slightly higher in radiotherapy arm(79% ±11% vs 64%±11%) ,it was not statistically significant(p:0,282).
Summary / Conclusion: The use of RT was associated with significant improvements in OS and PFS for all patients with DLBCL in previously reported studies.Although PFS was longer in radiotherapy group, it was not found to be statistically significant in our series.This results has to be assesed in prospective clinical trials.

Age	54(17-88)
Sex F/M	43/49
IPI 0/1/2/3/4/5	1/24/27/22/11/7
Stage 1/2/3/4	23/16/31/22
Bulky disease size 5-7 cm 7-10 cm >10 cm	 23 16 27
Radiotherapy 0/1	62/30
Response to CT CR/PR/Ref/NA	65/5/15/7

	Radiotherapy (n:22)	No Radiotherapy(n:43)	p
age	55(17-77)	44(20-81)	0,072
Sex F/M	11/11	21/22	0,929
Stage 1/2/3/4	10/6/4/2	8/7/18/10	0,031
IPI 0/1/2/3/4/5	0/12/6/2/1/1	1/8/17/12/4/1	0,067

B1628

A 10-YEAR SINGLE-CENTER EXPERIENCE IN PRIMARY GASTRIC DIFFUSE LARGE B CELL LYMPHOMA: FROM PRESENTATION TO TREATMENT AND PROGNOSIS

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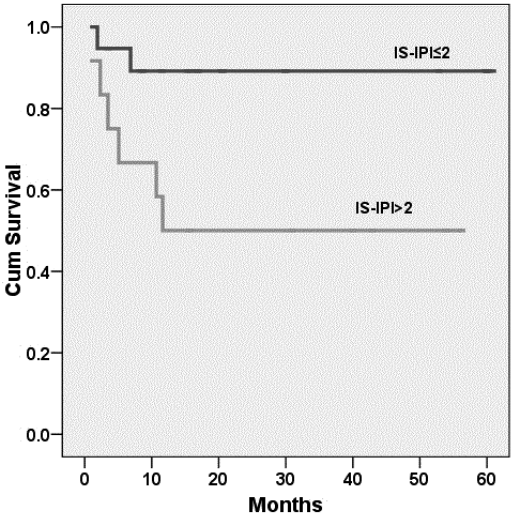
Background: Diffuse large B cell lymphoma (DLBCL) is a common subtype of non Hodgkin lymphomas (NHL), and its extranodal variant can arise from extranodal lymphatic tissue or non-lymphatic tissue. Primary gastric (PG) non Hodgkin lymphoma is a malignancy localized in the stomach with or without abdominal and/or extraabdominal lymph nodal involvement and constitutes 20-30% of all extranodal NHLs. Management of primary gastric diffuse large B cell lymphoma (PG-DLBCL) remains controversial as well as reliable staging system and prognostic factors. Few decades ago surgery has played a central role in the diagnosis, staging, and treatment of PG-DLBCL but adition of chemotherapy significantly improved survival. Since the availability of Rituximab, there is a lack of comparative studies investigating clinical effectiveness between surgery with immunochemotherapy and immunochemotherapy alone.
Aims: The aim of this study is to compare two treatments (immunochemotherapy alone and surgery plus immunochemotherapy) as well as to define most important prognostic factors.
Methods: Records of all-stages patients with a diagnosis of PG-DLBCL which were treated in the Clinic for Hematology Clinical Center of Serbia, between 2002 and 2012, were reviewed. Patients fulfilling the following criteria were included in this study: patients with histologically proven large-cell B lymphoma of the stomach who received Rituximab plus CHOP (R-CHOP) regimen as first-line immunochemotherapy with or without additional surgical resection.
Results: From 73 patients who were fulfilled inclusion criteria 44 received R-CHOP and 29 underwent surgical resection followed by R-CHOP. All clinical and pathological features were similar between the two groups. 45 patients (61,5%) had complete response to treatment, 11 (15,1%) had partial response to the treatment, 2 (2,7%) had stable disease and 15 (20,5%) had progressive disease. Tumor resection did not improve 5-years OS (75,9% and 65,9%, for surgery plus immunochemotherapy and immunochemotherapy alone, respectively, P=0.293). Ann Arbor clinical stage ≥II (P=0.047), ECOG≥2 (P=0.008),

IPI≥2 (P=0.038), stage-modified IPI (for II2 grade of the Lugano staging system) (P=0,036), trombocytosis > 450x10^9/l (P=0.001), level of CRP ≥5mg/l (P=0.028) and albumins level low than 28g/l (P=0.047) were predictors of OS in patients with PG- DLBCL. A new *inflammatory stage* IPI (IS-IPI) risk score (smIPI plus level of CRP) was recognized as the best prognostic tool (P=0,045) in multivariate analysis. There were significant differences among patients with low-risk (score 0,1,2) and intermediate/high-risk groups (score >2) in 5-years OS (89.5% vs 50.0%, P=0.021).
Summary / Conclusion: IPI staging system modified for high level inflammation has shown to be the best prognostic tool for overall survival of PG-DLBCL patients. Adition of tumor resection to immunochemotherapy did not improve survival. In preventing morbidity arising from early or late complications from surgery, immunochemotherapy should be a primary option for DLBCL of the stomach. To confirm clinical effectiveness of Rituximab beyond 5 years studies with longer follow up are needed.



B1629
DIFFUSE LARGE B CELL LYMPHOMA PRESENTING WITH OSSEOUS INVOLVEMENT, CLINICOPATHOLOGICAL CHARACTERIZATION AND SURVIVAL ANALYSIS
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Background: Primary diffuse large B cell lymphoma of bone is an extremely rare condition that is usually confused with other primary injuries of the bone.
Aims: we have thus conducted this retrospective analysis of our non Hodgkin lymphoma database to determine the clinicopathological and survival characteristics of this unusual presentation.
Methods: DLBCL patients treated at Cairo Oncology Centre (Cairo, Egypt) in the period between 2000-2008 were reviewed. Eligible patients were those who had complete information on date of diagnosis, histopathological and immunohistochemical confirmation of the diagnosis and received CHOP-like chemotherapy. We compared the difference in systemic therapy and pathological parameters between cases presenting with and without osseous involvement. We investigated the impact of osseous involvement on progression free survival (PFS) and overall survival (OS) in a Cox regression model adjusted for age, Ann Arbor stage, performance status, extranodal involvement, presence of B symptoms, IPI score and treatment.
Results: 240 DLBCL patients were included in the analysis fulfilling the inclusion criteria. Of which 21 patients only have definite radiological evidence of bone involvement (8.75%). Bone involvement was isolated in 5 cases, associated with nodal involvement in 4 cases and associated with both nodal and extranodal localization in 12 cases. Median age for the whole group is 53 years while for the bone involvement group it was 54 years. At a median follow up period of 13 months, the median PFS for the whole group was 79 months, for the osseous involvement group it was 34 months. Cases with bone involvement were more likely to have advanced stage (P=0.048), bone marrow involvement (P=0.004), higher IPI (P=0.043). Based on univariate analysis, bony involvement alone was not significantly associated with shorter PFS (P=0.202).while bone involvement was not significantly associated with other adverse clinicopathological factors (elevated LDH, B symptoms or bulky disease).
Summary / Conclusion: According to our data, patients with DLBCL presenting with bony involvement more often present with advanced stage, shorter median PFS and higher risk disease and should be considered for more aggressive treatment.

B1630
EVALUATION OF EFFICACY AND SAFETY OF BENDAMUSTINE TREATMENT IN OSAKA LYMPHOMA STUDY GROUP(OLSG) OF JAPAN
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Background: Bendamustine was approved in Japan in December, 2010 and used for the patients with relapsed or refractory indolent lymphoma.
Aims: In this study, we evaluated efficacy and safety of bendamustine in the practical use.
Methods: We analyzed the clinical data of 122 patients who were treated with bendamustine from December, 2010 to March, 2012 in OLSG.

Overall Response Rate (ORR)	BR combination (N=87)	B monotherapy (N=35)
CR/CRu	52 (59.8%)	15(42.9%)
PR	19 (21.8%)	8 (22.9%)
SD	8 (9.2%)	3 (8.6%)
PD	8 (9.2%)	8 (22.9%)
Unknown	-	1 (2.9%)
Prior B regimen numbers: ORR	*P<0.0001*	
1: CR+PR	38 (92.7%)	3 (100%)
1: SD	2 (4.9%)	-
1: PD	1 (2.4%)	-
2: CR+PR	14 (93.3%)	9 (69.2%)
2: PD	1 (6.7%)	4 (30.8%)
≧3:CR+PR	19 (61.2%)	11 (57.9%)
≧3: SD	6 (19.4%)	3 (15.8%)
≧3: PD	6 (19.4%)	4 (21.1%)

Results: The patients' ages were 36 and 90 (median: 68). The ratio of male to female was 52.5:47.5. The histological diagnoses were follicular lymphoma in 70.5% and mantle cell lymphoma in 18.9%. Bendamustine was used in combination with rituximab in 71.3% of cases. The other cases were treated with bendamustine monotherapy. The completion of the planned regimen (six cycles) was done in 29.5%, while the other caseswere discontinued therapy due to the adverse events (36.0%), PD (22.1%) and achievement of CR (24.4%). Regarding response, 59.8% of CR and 21.8% of PR were achieved in combination with rituximab, while 42.9% of CR and 22.9% of PR were achieved with bendamustine monotherapy. CR+PR were achieved in 93.2%, 82.1% and 56.0% of the patients whose prior treatment regimen number were one, two andmore than three respectively. The progression-free survival of the patients treated with bendamustine-rituximab combination was significantly better than bendamustine monotherapy (P=0.0457).The multivariate analysis showed that three factors (sex, serum LDH level and prior treatment regimen number) were prognostic; female, low LDH and one or two prior regimen were favorable factors. Regarding toxicity, the hematological adverse event (HAE)(Grade 4) was observed in 71.3% and non-HAE (Grade3, 4) was observed in 12.6% with bendamustine-rituximab combination, while in 60.0% and 11.4% respectively with bendamustine monotherapy. Furthermore, febrile neutropenia (Grade3, 4) was

observed in higher number of cases with bendamustine-rituximab combination than with bendamustine monotherapy.
Summary / Conclusion: Bendamustine was quite effective for the patients with relapsed or refractory indolent B-cell lymphoma. The early use of bendamustine-rituximab combination was supposed to be more effective. However, the combination use caused the more severe toxicity. It is necessary to clarify the best dosage of bendamustine in combination with rituximab expecting the best efficacy and safety in the future study.

B1631
PREDICTING FACTORS FOR GLUCOCORTICOID INDUCED-DIABETES MELLITUS IN DIFFUSE LARGE B-CELL LYMPHOMA PATIENTS WHO RECEIVED R-CHOP CHEMOTHERAPY
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Background: Glucocorticoids are widely used in treatment of patients with lymphoma in combination with chemotherapy agents, but development of hyperglycemia is one of the major problems. Avoidance of unnecessary tests for screening of glucocorticoid-induced diabetes mellitus (GDM) might improve the quality of life during chemotherapies for patients with lymphoma.
Aims: To evaluate predicting factors for GDM in patients with diffuse large B cell lymphomas (DLBCL) who received R-CHOP chemotherapy.
Methods: A total of 46 patients with DLBCL who received chemotherapy with R-CHOP regimen in University of Tsukuba Hospital from November 2006 to June 2012 were analyzed. Patients with previous diagnosed DM were excluded. Diagnosis of DM was based on the American Diabetes Association's criteria with, fasting plasma glucose (FPG) □ 126 mg/dL or a random plasma glucose □ 200 mg/dL accompanied by classic symptoms of hyperglycemia. Metabolic syndrome was defined by the criteria of the International Diabetes Federation, with body mass index (BMI) > 30 kg/m^2 and any two of the following: 1) raised triglycerides > 150 mg/dL; 2) reduced HDL cholesterol < 40 mg/dL in males, < 50 mg/dL in females, or specific treatment for this lipid abnormality; 3) systolic blood pressure (SBP) > 130 mm Hg or diastolic BP (DBP) > 85 mm Hg. All described values of Hemoglobin A1c (HbA1c) in this study are expressed in HbA1c, NGSP. Univariate analysis was perfromed by chi-square test, and linear logistic regression analysis was used for multivariate analysis.
Results: Total number of patients diagnosed as GDM during R-CHOP chemotherapy was 14 of 46 patients (30.4%). Median total cycle number of chemotherapy was6, and 9 of 14 patients with GDM (64.2%) were diagnosed during the 1st cycle. 3 of 14 patients with GDM were managed with insulin, 1 was with exercise and diet therapy, and rest of patients received no therapy. No acute complications of hyperglycemia were observed. Pre-chemotherapy factors significantly associated with GDM were turned out to be HbA1c level more than 5.8 percent (P<.05), metabolic syndrome (P<.05), and previous history of hypertension (HTN) or elevated BP (SBP> 130 mmHg, DBP> 85 mmHg) at the start of R-CHOP regimen (P<.05) with univariate analysis. By the multivariate analysis, HbA1c level more than 5.8 percent (P<.05, RR = 5.4, CI: .1.29- 22.6) and history of HTN or elevated BP (p =.054, RR = 4.33, CI: .97-19.3) were the independently significant factors associated with GDM.
Summary / Conclusion: DLBCL patients with HbA1c level more than 5.8 percent or elevated BP or history of HTN at the start of R-CHOP regimen would be possible indications to check plasma glucose level during the chemotherapy to seek out GDM.

B1632
PROGNOSTIC SIGNIFICANCE OF LOW LYMPHOCYTES COUNT IN THE PATIENTS WITH DIFFUSE LARGE B CELL LYMPHOMA (DLBCL)
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Background: Lymphocytes are target for immunochemotherapy and their number is an indicator of immunological status. It was previously reported that low lymphocyte count has a prognostic significance in the patients with diffuse large B cell lymphoma (DLBCL).
Aims: The present study was designed to investigate the clinical and prognostic significance of low lymphocyte count in our group of patients with DLBCL.
Methods: We retrospectively analysed prognostic significance of low lymphocytes count at the time of diagnosis in 277 DLBCL patients. There were 203 nodal and 74 extranodal DLBCL. Only the patients treated with immunochemotherapy (CHOP or CHOP-like chemotherapy plus rituximab) were included in the study. Cut off for low lymphocytes count was determined by ROC analysis.The prognostic values of absolute lymphocyte count with respect to overall survival (OS) and progression-free survival (PFS) were evaluatedby Chi-Square test and two-tailed log-rank test.Correlation of lymphocytes count with clinical parameters was also analysed.
Results: Median of lymphocyte count was 1.4x10^9/L (range 0,2-4.9x10^9/L). However, ROC analysis showed that optimal cut off of low lymphocyte count with the best sensitivity and specificity is 1.3x10^9/L. According to ROC analysis low lymphocyte count was found in 121 (43.32%) patients. There was significant statistical correlation between low lymphocyte count and elevated LDH (P=0.01) and "bulky" disease (P=0.001). Low lymphocyte count (1.3x10^9/L) was in significant correlation with event-free survival (EFS, P=0.014) and overall survival (OS) (P=0.04). Namely, median of survival of the patients with normal lymphocyte count was not achieved and in the group of the patients with low lymphocyte count is 23,9 months. On the contrary, low lymphocyte count was not associated with therapy response (P=0,089). A multivariate analysis revealed that only IPI remained associated with OS (P<0.01; HR, 4.286; 95% CI, 1.998 to 9.194). Similar results were found when nodal and extranodal lymphoma were analysed separately.
Summary / Conclusion: Low lymphocyte count is in significant correlation with EFS and OS of patients with CDLBL and can be used as prognostic factor in DLBCL.

B1633
MYOCET IN LYMPHOMA THERAPY: AN OBSERVATIONAL STUDY IN WESTERN AUSTRIA.
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Background: Anthracyclines play the major role within polychemotherapy. Liposomal non-pegylated doxorubicin (Myocet) is characterized by a better cardiac tolerance.
Aims: Aim of the study is the characterization of benefit and side effects of COMP in lymphoma, a CHOP-like regimen containing Myocet in real-life-setting.
Methods: 121 patients (m/w 73/48) were analyzed retrospectively by firstly characteristics of patients, and secondly details of COMP-like therapy including outcome and side effects.
Results: Median age, 73 years (26-88); adverse performance status (ECOG ≥2), 46 patients (38%); any cardiac comorbidity, 73 patients (60%). Histology of lymphoma: DLBCL 61%; MCL 12%, follicular lymphoma 9%; CLL 7%; peripheral T-NHL 7%; other NHL 4%. 89 patients (74%) received Myocet-based therapy (±rituximab) in first line, 16 (13%) in second line, and 16 (13%) in third or higher line. Median 6 cycles (1-8) were administered. 7 patients were withdrawn prematurely, 12 patients (11%) died during therapy, among them three with cardiac fatality. The response rate (CR+RR) in evaluable patients was 66% (70/106 pts) and 75% (6/8 patients) in B- and T-NHL, respectively. Response was associated with therapy line (74% in first vs 47% in higher line, P = 0.007). Grad III/IV neutropenia was found in 45%, whereby this was not dependent on therapy line. Survival data will be presented at the conference.
Summary / Conclusion: Myocet-based therapy is highly effective in therapy of lymphoma in difficult situations. Cardiac toxicity (seen during therapy at 11 patients) was not associated with preexisting cardial comorbidity.

B1634
PRELUDE: A PHASE 3 STUDY IN PROGRESS TO INVESTIGATE THE PREVENTION OF RELAPSE IN DIFFUSE LARGE B-CELL LYMPHOMA USING DAILY ENZASTAURIN
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Background: Despite the advent of rituximab-based immunochemotherapy, treatment outcomes for patients with high-risk (International Prognostic Index [IPI] score 3-5) diffuse large B-cell lymphoma (DLBCL) continue to be suboptimal with relapse rates at 2 years of 25% or more, even for patients in remission after first-line therapy. Overexpression of protein kinase C (PKC)β, a protein involved in the B-cell receptor signaling pathway, appears to be a poor prognostic marker in patients with DLBCL (Shipp et al. *Nat Med*. 2002;8:68-74). Enzastaurin, a potent, selective inhibitor of PKCβ, has demonstrated clinical activity in a subset of relapsed patients with DLBCL and has a favorable safety profile.
Aims: Based on these results, a Phase 3 trial was initiated to investigate the efficacy of enzastaurin in patients who have achieved complete remission after standard first-line therapy.
Methods: Patients had histologically confirmed DLBCL with IPI score of 3-5 at diagnosis and had achieved a complete response or complete response-unconfirmed to cyclophosphamide, doxorubicin, vincristine, and prednisone, plus rituximab therapy. Patients were randomized in a 2:1 fashion to receive enzastaurin 500 mg daily (after a 375-mg loading dose 3 times daily on Day 1 only) or placebo. Treatment continued until patients developed progression of disease, unacceptable adverse events, or completed 3 years of therapy. All patients were followed for recurrence of disease and survival until death or study closure, whichever occurred first. The primary endpoint was overall disease-free survival (DFS). The trial was designed to have 80% power to detect a hazard ratio of 0.68. The secondary endpoints were event-free survival (EFS), EFS rate at 2 years, DFS rate at 2 years, overall survival, safety, health-related quality of life using the FACT-Lym, health status using the EQ-5D scale, assessments of biomarkers, and pharmacokinetics.
Results: Trial in progress.
Summary / Conclusion: The trial completed patient enrollment (N=757) in April 2010. Two interim analyses were performed by an independent data monitoring committee, with the recommendation to continue the trial. Final results will be analyzed after the last treated patient has been followed for 3 years.

B1635

FOLLICULAR LYMPHOMA IN FIRST RELAPSE: ANEMIA AND HIGH ERYTHROCYTE SEDIMENTATION STRONGLY PREDICT THE OUTCOME

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Background: The prognosis of patients with follicular lymphoma (FL) significantly improved after adding rituximab in treatment plan of these patients, both for newly diagnosed and relapsed patients. FLIPI and FLIPI2, widely accepted prognostic indices in FL were primarily designed for patients with newly diagnosed disease. Nowadays, the precise risk assessment also in relapsed FL patients seems to be necessary, since lot of treatment strategies are available for these patients, less or more agressive.
Aims: The aim of this study was to analyze the prognostic value of routinely determined clinical and laboratory parameters in patients with first relapse of follicular lymphoma.
Methods: The retrospective analysis was performed on 60 patients with diagnosed first relapse of FL grade I, II or IIIa, in the period February 2002-April 2010. In the first line, the patients were treated with R±CHOP or R±CVP. All the patients in the first relapse were treated with fludarabine based regimens (FC, FND), of whom 33 patients in combination with rituximab. The characteristics in first relapse examined as possible risk factors were age, higher hystological grade in relapse, presence of B symptoms, presence of "bulky" tumor (>10 cm in diameter), spleen enlargement, high FLIPI score, anemia (Hgb<12 g/dL), LDH level and erythrocyte sedimentation rate (ESR). Receiver operating curve was used to determine the optimal cutoff value for ESR in prediction of overall survival (OS) for our group of patients. Survival functions were estimated using the Kaplan-Meier method and compared using the log-rank test. A multivariate analysis was performed to evaluate the potential predictive value of the examined characteristics as a risk factor.
Results: The median follow up was 32 months (range 4-115 months). In first relapse, 24 (40%) patients were older than 60 years. Higher histological grade in relapse, B symptoms, bulky disease, spleen enlargement, high FLIPI score, anemia, elevated LDH and ESR>25 mm/h were present in 17 (28.3%), 41 (68.3%), 23 (38.3%), 32 (53.3%), 36 (60%), 20 (33.3%), 26% (43.3%) and 33 (55%) patients, respectively. The patients with B symptoms, high FLIPI score, anemia, and ESR>25 mm/h had significantly worse OS (P=0.000; P=0.001; P=0.003; P=0.000, respectively), while there was a trend toward worse OS in elderly patients (P=0.065) and patients with elevated LDH (P=0.091). Multivariate analysis identified anemia (P=0.034) and ESR>25 mm/h (P=0.005) as independent risk factors for poor outcome. Based on cumulative score of unfavorable prognostic factors identified in multivariate analysis, 2-years OS was significantly better (P=0.024) in patients who didn't have unfavorable factors (2-years OS 81.8% pts), compared to patients with 1 (2-years OS 60.9% pts) or 2 (2-years OS 40% pts) risk factors.
Summary / Conclusion: Modern clinical researches are having the aim to individualize treatment approach based on risk for poor outcome. Our findings suggest that some FL patients in first relapse require more effective treatment. Having in mind that more aggressive treatments such as high dose therapy with stem cell transplantation are associated with higher toxicity, the optimal approach according to risk has to be defined in new prospective studies.

B1636

ORBITAL AND OCULAR ADNEXAL MALT (MUCOSA-ASSOCIATED LYMPHOID TISSUE) LYMPHOMAS, TEN YEAR EXPERIENCE

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Background: Orbital and ocular adnexal Non Hodgkin Lymphomas (NHL) consist 2% of all NHL. The most frequent hystological sybtipe is extranodal marginal zone B cell lymphoma, MALT (Mucosa-Associated Lymphoid Tissue). Autoimmune inflamatory disorders as well as chronic infections are important ethiological factors. Various local disease signs and simptoms can occur a long period of time prior to diagnosis. Immunohistochemical markers CD5 or CD43 (sialophorin) are important negative predictive factors. Various treatment modalities are available.
Aims: To investigate clinical and laboratory parameters of patients with ocular adnexal MALT lymphoma (OAML), to compare efficiency between different therapy modalities and to investigate disease outcome.
Methods: Seventeen patients with OAML, diagnosed in Clinic of Hematology, Clinical Centre of Serbia between 2003 and 2013, were inrolled. We researched epidemiologic-demographic, clinical and laboratory characteristics on presentation, importance of Helicobacter Pylori (Hp) infection, clinical stage of disease and prognostic value of CD43. Efficiency of various therapy modalities was compared.
Results: Highest disease incidence rate was in eight decade, it is almost 2.5 times more frequent in male population. Overall median age is 66 years (range 36-79), males 67.5 years (36-79), females 57 years (48-77). No significant statistic difference between age at diagnosis and patients gender was confirmed. Local signs and symptoms of the disease were present much earlier prior to diagnosis (median 8.9 months, range 3-36). Seven patients (53%) had orbital lymphomatous involvement, 4 (23%) conjuctival, 2 (12%) lacrimal gland, one (6%) eyelid and one (6%) uveal involvement. The most frequent sign on presentation was swelling of orbital tissue, conjuctiva or eyelid (7 patients, 33%). Observed laboratory parameters on presentation showed low disease activity: median sedimenation rate 12mm/h (range 2-24mm/h), mean lactat dehydrogenase 333.76U/l (range 200-409U/l), median C reactive protein 1.49mg/l (range 0.20-9.50mg/l) and median beta-2 microglobulin 1.96mg/l (range 1.39-5.60mg/l). A significant presence of Hp infection (66.67%) was recognized. Predictive significance of CD43 was not confirmed. CD5 was negative in all cases. All patients have had localised disease and were staged as IE CS (Ann Arbor lymphoma staging system). One patient had B simptomatology on presentation. Ten patients, aged ≥60 had low intermediate risk (International Prognostic Index, IPI), six aged <60 had low risk and one low intermediate risk (age adjusted IPI, aaIPI). In our group, 5 year progression free survival (PFS) is 60%. There was no significance in PFS between initialy used treatment modalities, surgery vs. chemiotherapy (P=0.9942), surgery vs. radiotherapy (P=0.8296) and chemotherapy vs. radiotherapy (P=0.9191). All patients after initial or relapse treatment achieved disease remissions. No significance was observed between cumulative radiotherapy dosage and treatment outcome. Seven patients (41.17%) had relapse. One patient died due to non-hematologic complications.
Summary / Conclusion: Our results confirms that OAML has good overall therapy response, regardless of initial or relapse treatment modality, as well as good progression free survival and overall survival rate.

B1637

HEPATITIS B REACTIVATION IN PATIENTS WITH NON HODGKIN LYMPHOMA CD 20+ IN MAINTENANCE THERAPY WITH RITUXIMAB

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Background: Anti CD20 antibody (Rituximab) based chemotherapy regimens increase the HBV reactivation risk although sporadic HBV reactivation cases are reported in patients on maintenance with Rituximab single therapy too.
We evaluated how many HBV reactivation occurred among patients Hepatitis B core antigen positive (HBcAB +) and Hepatitis B surface antigen negative (HBsAg-) who received Rituximab single therapy during maintenance.
Aims: The aim of this study is to assess the prevalence of HBV reactivation among patients HBcAb +/ HBsAg – during the maintenance therapy with Rituximab.
Methods: In our Unit, 88 patients with non Hodgkin Lymphoma CD20+ received maintenance therapy with Rituximab (schedule: 375 mg/mq every 3 months for 2 years) from January 2007 to February 2013.
Patients were treated with different chemotherapy regimens: 40% (35/88) with R-CHOP; 52% (46/88) with R-FN; 3%(3/88) with R-F; 5% (4/88) with R-Leukeran. None of these patients received prophylactic therapy with lamivudine during induction or maintenance.
All the patients were given blood tests for HBV (HBsAg; HBsAb; HBeAg; HBeAb; HBcAb) before starting maintenance therapy and liver function tests before each administration of Rituximab.
Results: 20% of the patients (18/88) were HBcAb positive.
64% of the patients (56/88) completed the maintenance treatment: one of thesepatientsoccurred the HBV reactivation.
36% of the patients (32/88) arestillintherapy with Rituximab and 9% of them are HBcAb positive (3/32): all thesepatientsare at risk for HBV reactivation too.
Summary / Conclusion: Inpatients HBcAb +/ HBsAg – treatedwithRituximab in single therapy is indicated the prophylaxiswithlamivudine.
In our observational study the HBcAb +/ HBsAg- patients didn't receive prophylactic therapy with lamivudine during the maintenance therapy with Rituximab and the HBV reactivation occurred in one patient HBcAb+/HBsAg- three months after the end of the maintenance therapy (1/18).
More ambitious prospective studies are required to establish theclinical utility-of prophylactic therapy with lamivudine during the maintenance therapy with Rituximab.

B1638

GOOD PROGNOSIS IN PRIMARY HEPATIC LYMPHOMA WITH OR WITHOUT HCV INFECTION

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Background: Primary hepatic lymphoma (PHL) is an uncommon lymphoid tumor frequently associated with a poor prognosis. PHL was first described in 1965 by Ata *el al* and in 1986 Caccamo et al defined PHL as a lymphoma localized and limited to the liver without extrahepatic involvement. To date, less than 150 cases have been published.
Aims: We report 11 patients with PHL diagnosed from 1995 to 2011 in our center, with a study of the viral status and the result of cytotoxic treatment.
Results: Eleven patients with PHL were identified. The disease occurred in middle-aged men (median age: 58 years). The main presenting complaint was right upper quadrant abdominal pain (4/11 patients). Tumor markers (α-fetoprotein and CEA) were normal in 8 patients tested. Liver scans demonstrated either a solitary nodule or multiple lesions. Pathologic examination revealed diffuse large B cell lymphoma in six patients, one case of follicular lymphoma, one of small lymphocytic lymphoma and one case of T cell lymphoma. Eigth patients (72%) were HCV-positive. Eigth patients received chemotherapy with CHOP regimen (6CHOP, 2 R-CHOP), two patients received R-FN, while a patient with a single focal lesion received surgical treatment. The complete remission rate was 100% (11/11); one of these patients, who had HCV-related cirrhosis, died because of hepato-renal syndrome, and another one died because of Acute Myeloid Leukemia.
Summary / Conclusion: The outcome of patients with PHL who are treated with combination chemotherapy seems excellent. The frequent association of PHL with HCV infection suggests a possible role of this virus in lymphomagenesis. HCV- infection does not appear to influence the outcome of therapy.

B1639

MODIFIED VIGEPP PROTOCOLE AS A NEW SALVAGE REGIMEN FOR RELAPSED REFRACTORY LYMPHOMA PATIENTS

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Background: Salvage chemotherapy followed by high dose therapy and autologus stem cell transplantation(ASCT) is the standart treatment for relapsed/refractory Hodgkin and Non Hodgkin lymphoma patients.Response of these patients to salvage chemotherapy protocols predict outcomes after ASCT.Currently, the optimum salvage therapy is still not known; platinum,mitoxantron,ifosfamide or gemcitabine based regimens can be preferred according to the patient characteristics.
Aims: We aimed to share our results with a new salvage regimen 'modified ViGePP protocole' in relapsed/refractory Hodgkin/Non Hodgkin lymphoma patients.

Diagnosis(n) NHL HL	6 16
Median age	39(17-63)
Gender(male/female)	12/10
Stage before ViGePP(n:) Stage 1 /2/3/4	1/5/7/9
Disease status before ViGePP (n) Relapse Primary refractory	14 8
Number of salvage treatment before ViGePP(n) 1 line 2 line >2line	4 12 6
Number of ViGePP courses(n) 1/2/3	2/18/2
Response to 2 cycles ofViGePP (n) CR/PR/Refractory	2/10/7
Auto transplant before/after ViGePP(n) **Allo transplant after ViGePP(n)**	3/9 3
Current status (alive /exitus)	15/7

Methods: We retrospectively analyzed 22 relapsed /refractory Hodgkin/Non Hodgkin lymphoma patients who were treated with modified 'ViGePP' salvage regimen' in Ankara Oncology Hospital. Demographic features and clinical variables of patients are summarized in Table 1. All of the patients had been treated with two or three cycles of modified ViGePP chemotherapy either as first line salvage regimen or after multiple lines of different regimens.Three patients were treated with this regimen for relapse after ASCT.Chemotherapy protocol consisted of vinorelbine 25 mg /m^2 gemcitabine 800 mg /m2 in 1. and 8.days, oral (PO) prokarbazin 100 mg/m^2 1-7 days and oral prednisone 60 mg /m^2 1-15.days. Response assesment has been performed after 2 courses of regimen except 3 patients who had only 1 course
Results: Median time period between diagnosis to ViGePP treatment was 32 (6-179) months. Overall response rate after 2 courses of chemotherapy was 60% (12/20, CR(n:2)+PR(n:10)). Treatment related mortality was 13% (3/22).We observed 18% grade 3 neutropenia,31% grade 4 neutropenia,22 % grade 3 thrombocytopenia, 13 % grade 4 thrombocytopenia.There were no nonhematological toxicities over grade 1.Ten patients were mobilized with filgrastim alone (n:5), after ViGePP regimen(n:4) or after plerixafor (n:1).Median time from the beginning of the treatment to ASCT was 4.5 (2-10) months. Nine patients who had ASCT has been followed in remission (1 PR/8 CR).Three patients who had relapsed after ASCT were treated with ViGePP followed with allogeneic SCT.One year overall survival of all patients was 74%±11%.
Summary / Conclusion: ViGePP salvage regimen has similar response rates with other chemotherapy protocoles without high treatment related toxicity rates.Although our number of patients mobilized with this regimen are low ,we think that it has high mobilization success rates.So we conclude that,it can be used easily as a bridge to transplantation for relapsed/refractory Hodgkin /Non Hodgkin lymphoma patients.

B1640

DIFFUSE LARGE B CELL LYMPHOMA (DLBCL) COEXISTENT WITH HEPATITIS C INFECTION; SINGLE INSTITUTIONAL EXPERIENCE FROM EGYPT

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Background: Hepatitis C is a major health problem in Egypt and many European and North African countries; and cases of DLBCL co existing with HCV positive infection are increasingly encountered.
Aims: So, we have conducted this retrospective analysis of our non hodgkin lymphoma database to clarify the clinicopathological and survival characters of cases with coexistent HCV infection and DLBCL.
Methods: DLBCL patients treated at Cairo Oncology Centre (Cairo, Egypt) in the period between 2000-2008 were reviewed. Eligible patients were those who had complete information on date of diagnosis, histopathological and immunohistochemical confirmation of the diagnosis and received CHOP-like chemotherapy. We compared the difference in systemic therapy and patholog-

ical parameters between cases that are hepatitis C antibody (HCV Ab) positive and cases that are not. We investigated the impact of HCV positive status on treatment toxicity and progression free survival (PFS) and overall survival (OS) in a Cox regression model adjusted for age, Ann Arbor stage, performance status, extranodal involvement, presence of B symptoms and treatment.
Results: 230 patients were included in the analysis fulfilling the inclusion criteria. 17 patients were confirmed to be HCV Ab positive whilst the rest of the cases were either negative or unknown. At a median follow up period of 13 months, the median PFS for the whole group was 12.03 months, while for the HCV Ab +ve group it was 8.48; the median OS for the whole group is 13.2 months while for the the HCVAb +ve subgroup it was 8.48 months. ther ewas no statistically significant correlation between HCV positive status and any adverse prognostic indicator like extranodal presentation (P=0.34),B symptoms(P=0.33),elevated LDH (P=0.54) or age>60 years (P=0.32). Based on univariate analysis, HCV Ab +ve status was not associated with shorter PFS (P=0.65). Treatment was tolerated in the majority of HCV Ab +ve patients with only 2 patients showing grade 2 liver dysfunction with treatment.
Summary / Conclusion: According to our data, patients with DLBCL coexistent with HCV infection should be managed in the same way as other DLBCL cases .however, more frequent monitoring of liver function and PCR status and multidiciplinary discussion with the hepatologists is required .

B1641
SAFETY OF BENDAMUSTINA INCLUDING DHAP REGIMEN AS SALVAGE THERAPY IN MULTIRESISTANT LYMPHOMA PATIENTS
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Background: The management of patients (pts) with lymphoma recurring after stem cell transplantation or multiply relapsed disease remains challenging. Many studies have demonstrated the efficacy and safety of Bendamustine combinations in heavily pretreated pts.
Aims: Our study was designed to assess the safety of Bendamustine including DHAP regimen as salvage therapy in pts with refractory/relapsed lymphomas.
Methods: Ten patients were treated at 4-weekly intervals with Bendamustine 90 mg/mq on days1,2; Cisplatin 100 mg/mq over 24 hours on day 2; Cytarabine 2000 mg/mq (two doses) on day 3; Dexamethasone 40 mg on days 1–4 with or without Rituximab 375 mg/mq on day +4. Palonosetron was given as antiemetic prophylaxis on days1,3. A daily G-CSF was admistered starting by day +6 in 4 patients while a pegilated G-CSF was used in 6 patients on day +5. A total of 22 courses were administered and each patient received at least 2 cycles of therapy. The patient's characteristics are shown in table 1. At the time of enrollment 8 pts had a progressive disease.
Results: Chemotherapy-induced grade 1 nausea and vomiting were observed in 4 pts, mainly on days 3 and/or 4. Grade 3 and 4 haematological toxicity consisted of anaemia (3 pts), neutropenia (7 pts) and thrombocytopenia (6 pts). Severe neutropenia and thrombocytopenia were recorded mainly between days +10 and +14 with haematological engraftment (Neutrophils>500/mmc and Platelets>20.000/mmc) after a median of 4 days (range 3-6 days) from the nadir. Three patients had a febrile neutropenia requiring hospitalization and two died because of K. Pneumoniae sepsis. No grade 3 and 4 extra-haematological toxicity was observed. Eight patients are still on therapy.

PARAMETERS		N°
Histological subtypes	HL	4
	DLBCL	1
	PTCL	1
	SMZL	2
	RICHTER	1
	FL	1
Primary Refractory Disease		5
Relapse After ASCT		2
Prior Lines of Chemotherapy≥2		3
Disease Status at Enrollment	Progressive Disease	8
	Partial Response	2
Age Median (range)	53 years	(26-77)

Summary / Conclusion: In our experience, despite patients had multidrug-resistant disease heavily pretreated, the addition of Bendamustine to DHAP regimen seems safe with an acceptable toxicity profile if compared with an historical control group of patients treated at our Institute with DHAP alone. The two patients died due to a sepsis had a primary refractory disease relapsed after ASCT. Survival and response rate analysis, as well as the mobilizing potential of this Bendamustine combination can not be evaluated because of the small number of patients and the short follow-up. We are increasing our series and we hope to be able to present these results further on.

B1642
SPINAL CORD COMPRESSION AS THE INITIAL MANIFESTATION OF B- CELL LYMPHOMA: A CLINICO PATHOLOGICAL REVIEW OF 11 CASES
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Background: In patients with non-Hodgkin's lymphoma (NHL), inaugural spinal cord compression is rare and thought to occur in less than 5% of cases. Even in major centers experience of this entity is modest and optimal treatment thus remains unclear. We retrospectively studied 11 patients who had B-cell lymphoma revealed by spinal cord compression symptoms.
Aims: The aim of this study is to study the epidemiological features and clinical outcome of B-cell lymphoma revealed by spinal cord compression.
Results: We reviewed departmental records covering the 6 years period from 2006 to 2012 and we identified 11 patients presenting with spinal cord compression as their first manifestation of NHL.
They were 6 men and 5 women in this series. Patients ranged from 32 to 82 years of age with a median of 62 years old. Tumor lesions involved the thoracic spine in 4 cases, and the lumbar spine in 7 cases. At presentation 6 patients were non-ambulatory. Dual sphincter impairment was found in 4 patients. Bladder dysfunction was noted in 3 cases only. The pathology study showed two cases with low-grade lymphoma: lymphocytic lymphoma and follicular lymphoma and 9 cases with diffuse large B cell lymphoma. On admission; there were 3 cases in PS=0-1, 4 cases in PS=2 and 4 cases in PS=3. Serum lactate dehydrogenase (LDH) was normal in 7 cases and high in 4 cases. Seven had advanced stage at diagnosis, while 4 had limited disease: including three with localized epidural lymphoma and one with primary bone lymphoma. Nine patients underwent laminectomy for decompression and tissue diagnosis, after which 2 underwent radiotherapy, 2 underwent chemotherapy, and 7 underwent combined-modality treatment. The functional outcome was improvement in all cases, no patient worsened after surgery. Tow patients had autologous peripheral stem cell transplantation. All patients had early physiotherapy and achieved functional independence at the community ambulation level, even if paretic at presentation. The overall survival (OS) at 1 year was 81%. No difference in OS was noted between localized and advanced disease.
Summary / Conclusion: B-cell lymphomas are an uncommon cause of spinal cord compression. Functional outcome can be quite favorable, as can tumor outcome. Residual sensory deficits greater than motor deficits are not uncommon. The clinical and functional response of such patients to treatment and their more favorable overall prognosis emphasis the importance of an accurate histological diagnosis, full disease staging and the subsequent initiation of appropriate therapy.

B1643
EPIDEMIOLOGICAL DATA AND CLINICAL FEATURES OF 205 NON-HODGKIN LYMPHOMA PATIENTS AT A SINGLE CENTER IN TURKEY
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Background: There has been major progress in the diagnosis, classification, and treatment of nonHodgkin lymphoma (NHL).The distribution of NHL in various geographic regions might differ and certain subtypes might prevail in one area.
Aims: There is no data about the epidemiology of NHL in Turkey. We retrospectively determined the annual incidence of hospital-based NHL in Turkey based on patient registration data in our center in northwestern Turkey.We also report on clinical features, treatment modalities and outcomes, survival, prognostic factors.
Methods: We evaluated 205 NHL patients diagnosed between 2002-2011. Our hospital has been the only tertiary referral center for hematological diseases for a mixed rural and urban population of 616000 people for longer than 16 years (316000 males, 300000 females). Patients' demographic and clinical features, treatment modalities, and responses were recorded.The current World Health Organization (WHO) classification was adopted for histopathological diagnosis. Response to therapy was based on 2007 International Workshop Criteria. For survival analysis, time from diagnosis until the end of follow-up or time to death were considered. Informed consent was obtained.
Results: Of 205 NHL patients,121 (59%) were males and 84 (41%) were

females (M/F=1.44).During the study period,the annual incidence rate for all NHL was 3.33/100000.The annual incidence in women was 2.8/100000, and in men it was 3.83/100000.At the end of 2011,the overall prevalence of NHL was 33.3 per 100000 population aged >16 years.The prevalence in men (38.3/100000) was higher than the prevalence in women (28/100000).The mean age was 58.4 years (range:15-87).Seventy patients (34.9%) had B symptoms, 39 (19%) had bulky disease,and 99 (48.3%) had extranodal involvement.An intermediate-to-high risk International Prognostic Index (IPI) score was present in 39% of the patients.Diffuse large B cell lymphoma (DLBCL) was the most common subtype (106 patients,52%). Other most frequent histologic subtypes were follicular (18 patients,8.8%), peripheral T-cell (15 patients,7.4%), and small lymphocytic (14 patients, 6.9%) lymphomas. For remission induction, CHOP and CHOP-like regimens were used in 66 patients (32.2%), while R-CHOP was used in 61 patients (30%). For DLBCL patients, in intent-to-treat analysis, the overall response and complete remission rates were, respectively, 60.4% and 43.4%. During a 10-year period, 78 NHL patients died. The median survival was 41 months. Five and 10-year survivals were, respectively, 45% and 25%. NHL patients with B symptoms (28 vs. 60 months,P=0.05), splenomegaly (26 vs. 60 months,P=0.048), intermediate-to-high IPI scores (20 vs. 86 months,P=0.002), high β-2 microglobulin (26 vs. 96 months,P=0.024), and those with bone marrow involvement (26 months vs. unreached,P=0.005) at initial diagnosis had significantly worse prognosis than others. NHL patients who obtained complete remission with first line therapy had significantly longer median survival than patients who obtained partial remission or who were refractory (p values<0.001).

Summary / Conclusion: The incidence of NHL according to our hospital-based data was similar to the incidence in western registries. The most frequent histopathologic subgroup was DLBCL. NHL patients who had poor prognosis were those with B symptoms, intermediate-to-high IPI scores, and bone marrow involvement at initial diagnosis.

B1644

PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) HAVING DEVELOPED MALIGNANT LYMPHOMAS. COMPLETE REMISSION OF LYMPHOMA FOLLOWING RITUXIMAB-CONTAINING THERAPY, BUT NOT OF SLE.

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Background: The development of malignant lymphomas, generally of the non-Hodgkin type (NHL), and with a preference to diffuse large cell B lymphomas (DLCBL), in systemic lupus erythematosus (SLE), has been proven and analyzed in an exhaustive recent literature. The combination of germline and somatic mutations, persistent immune overstimulation and the impairment of immune surveillance facilitated by immunosuppressive drugs, is thought to be at the origin of the increased lymphoma genesis. However the treatment and course of such affected patients is less known, and prognosis is generally estimated as poor.

Aims: Out of more than 500 patients with complete/incomplete lupus and secondary antiphospholipid syndrome (APS) seen and treated at the institutional Day Hospital between 1982 and 2009, 9 developed lymphomas (5 DLCBL, 1 Hodgkin's, 1 follicular lymphoma and 1 indolent lymphocitic lymphoma).

Methods: Eight patients were treated with Rituximab-containing regimen

Results: All patients achieved complete remissions (CR) with a follow-up comprised between 18 and 190 months. In a patient with DLCBL was documented relapse,that was fatal.Two patients achieved complete remission (CR) of both diseases. In the other 5 lupus serology (ANA, APA) persisted, with occasional lupus flares and vascular complications.

Summary / Conclusion: While eradication of the last cancer stem cell is tantamount to cure in neoplastic disease, persistent autoantigenic overstimulation may contribute to the refractoriness of autoimmunity. This analysis proposes the institution of clinical trials with the use of rituximab and stem cell transplantation in the treatment of autoimmune diseases.

B1645

FOLLICULAR LYMPHOMA IN SITU: SERIES OF 8 CASES

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Background: Follicular lymphoma in situ (FLIS or follicular lymphoma-like cells of uncertain biological significance) is a rare lymphoproliferative disorder defined as colonisation of germinal centers by Bcl2 and CD10 overexpresing B cells. Follicular architecture is usualy preserved, so immunohistochemistry (in particular Bcl2 and CD10) and/or molecular work-up is needed for diagnosis. Clinical significance of FLIS is still obscure. Some cases are found either prior or next to overt lymphoma, or sinchronously with other solid tumors, while some are incidental findings.

Aims: Here we present a series of 8 FLIS cases diagnosed in our institution during the period from July 2010 to January 2013.

Methods: H&E and immunohistochemical staining were performed on routine fomalin-fixed paraffin-embeded lymph node specimens. Immunohistochemical panel included Bcl2 and CD10 markers. t(14;18) FISH analysis was performed using Vysis LSI BCL2 Dual Color Break Apart Rearrangement Probe. Clinical data was available in 5 cases.

Results: One patient had a history of microsatelite instable colonic carcinoma and squamous cell carcinoma of the lung. Both paratracheal lymph node biopsy (performed for staging of lung cancer) and peribronchial lymph nodes in subsequent lobectomy specimen revealed lymph node involvement by FLIS. Two patients had overt lymphoma: one had FL lymphoma and FLIS in the same lymph node, while the other had FL transformed to DLBCL with FLIS in the otherwise uninvolved lymph node. Remaining 5 patients underwent diagnostic biopsies due to lymphadenopathy. The first patient had concomitant pneumonia and elevated LDH of 418 U/l (normal LDH <243 U/l). The second patient with subsequent diagnosis of viral hepatitis C had splenomegaly, pancytopenia, and elevated LDH (470 U/l). The third patient had hepatosplenomegaly, weight loss, fever and malaise, he died of unknown causes 1 month later. The remaining two patients had only lymphadenopathy and one had elevated LDH (254 U/l). On gross evaluation lymph nodes in these 5 cases measured from 0.9 cm to 1.9 cm in greatest dimension. FLIS-involved lymphoid follicles were populated by homogeneous centrocyte-like cells with strong immunohistochemical Bcl2 and CD10 expression while demonstrating fairly preserved tissue architecture. Two out of 5 cases also demonstrated Bcl2 break by FISH analysis.

Summary / Conclusion: Our case series represents different clinical scenarios in which FLIS can be encountered. Though sometimes FLIS was just an incidental finding in cases of synchronous or metachronous lymphoma or solid tumor, 5 out of 8 cases demonstrated that FLIS alone can cause clinicaly suspicious lymphadenopathy leading to lymph node biopsy. To detect FLIS, routine minimal immunohistochemical panel should include Bcl2 and CD10. Close clinical follow up may be indicated for the early diagnosis of overt lymphoma in FLIS cases.

B1646

LYMPHOMA (HODGKIN AND NON-HODGKIN): EPIDEMIOLOGICAL FEATURES IN THE SOUTH EAST OF ALGERIA

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Background: In Western countries: non Hodgkin lymphoma (NHL) represents approximately 85% of lymphomas, their incidence is increasing, and almost 50% are over 70 years old.
The Hodgkin lymphoma (HL) represents approximately 15% of lymphomas: incidence rates have been stable over last 20 years, nearly 70% are less than 50 years at diagnosis, and many people have even less than 30 years.

Aims: Also the goal of this work is a comparative epidemiological study of lymphoma (HL and NHL) recruited in our area (south east of Algeria) over 4 years in the service and to extract their characteristics.

Methods: This is a retrospective comparative epidemiological study, based on the clinical data of patients (pts) diagnosed from January 2009 to December 2012. The diagnosis was confirmed by histological and immunohistochemical study.

Results: During this period, 253 patients with lymphoma were diagnosed, 127 NHL and 126 LH (50% each).The NHL are composed of aggressive NHL: 88 cases (69%), the most common sub type is diffuse large B-cell lymphoma (DLBC: 68%) and T/TNK (19%).The indolent NHL: 39 cases (30.7%); the most common is follicular lymphoma Comparing the epidemiological results found in the NHL with those in the HL we found: Cases/year: 32 versus 31. Median age: 54 versus 29 years. Frequency peak: (50-60) and (65-75), versus (20-30), knowing that 68% of pts with NHL are under the age of 60 years and75% of HL's pts have less than 50 years. Sex ratio (M/F): 0.98 versus 0.89. Notion of cancer in family: 12% versus 3%. Exposure to agriculture products: 9% versus 3%.

Summary / Conclusion: The epidemiological profile of lymphoma over 4 years in the south east of Algeria has some particularities: The LH and NHL; each occupies 50% of all diagnosed lymphoma. A parallel increase in the number of cases for the NHL and HL. The HL affects the young (median age = 29 years, 75% have less than 50 years) while the NHL is more observed in average age (median age=54 years, 68% are under the age of 60 years), this may be related to our young population. The majority of NHL diagnosed are aggressive (69%) with a predominance of DLCB lymphoma (68 %), and predominance of follicular and PCB (43% each) in indolent lymphoma. These data join the literature. These particularities are relevant and they must be the subject of deeper epidemiological and etiological investigations.

B1647

COMPARATIVE STUDY THE EFFICACY OF DIFFERENT ERYTHROPOIESIS-STIMULATING AGENTS IN ANEMIC PATIENTS WITH LYMPHOPROLIFERATIVE DISORDERS

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Background: Anemia in lymphoproliferative disorders (LPD) patients is a frequent symptom and can decrease the efficacy of antitumor chemotherapy, survival rate and overall quality of life (QoL). Pathogenesis of anemia in LPD patients is based on suppression by proinflammatory cytokines, decreasing erythroid precursor's sensitivity to serum erythropoietin and effect of chemotherapy. Therefore erythropoiesis-stimulating agents (ESA) are used as a pathogenetic therapy of anemia in patients with LPD which significantly increase hemoglobin, reduce and prevent RBC transfusions and improve QoL.
Aims: To study the efficacy of different ESA in anemia patients with LPD.
Methods: To our interventional prospective study were included the LPD patients (n=114): low-grade non-Hodgkin's lymphoma (n=17), chronic lymphocytic leukemia (n=26) and multiple myeloma (n=71). The median age of patients was 67 years (range 24-85). All patients had been received two or more cycles of antitumor chemotherapy before they were administrated ESA treatment. Every patient was observed anemia with initial Hb ≤10.0 g/dl. RBC transfusions were administrated to patients whose Hb concentration was <8.0 g/dl until level of Hb was increased up to 8.0-9.5 g/dl. We compared the efficacy of different ESA: Epoetin alfa (n=59), Epoetine beta (n=29), Darbepoetin alfa (n=26). All ESA were administrated to the patients subcutaneously, Epoietine alpha and beta – 150 IU/kg body weight 3 times a week and Darbepoietine alpha – 6.75 µg/kg b/w once per 3 weeks. The target Hb level was 11 g/dl. The planning duration of ESA treatment was within 16 weeks. Positive response was estimated as increasing Hb concentrating ≥2.0 g/dl or achieving target Hb level (11 g/dl).
Results: In the whole group of LPD patients mean baseline Hb concentration was 8.66±1.63 g/dl (3.7-10.0 g/dl). Before ESA-treatment 29 patients had received 2-12 units (median 3) of RBC transfusions during last 2-6 months because of low Hb (3.7-8.0 g/dl). The period of ESA-treatment was from 4 to 24 weeks (mean 9.6±4.6 weeks). During the study period 12 patients (41.4%) followed RBC transfusions after ESA-treatment and 17 patients (58.6%) showed transfusion-independency and 8 new patients began receiving transfusion first time as a result of the anemia progressing. On the whole we observed positive response in 78 patients (68.4%), their Hb concentration increased from baseline to 12.1±1.2 g/dl (11.0-15.7 g/dl; P<0.001) and in group patients with positive response reduced such symptoms as: feeling fatigue, weakness all over, having trouble starting things because of tiredness, depression, drowsiness, giddiness, headaches, pain in thorax and dyspnea. The comparison of efficacy ESA-treatment showed insignificant difference between all ESA. So patients received Epoetin alfa positive response observed 40/59 patients, Epoetin beta positive response – 20/29 and Darbepoetin alfa positive response – 18/26, that is showed similar results (67.8%, 68.9%, 69.2%, respectively) without statistical difference (P>0.1).
Summary / Conclusion: In this study was shown that all ESA is effective reducing symptoms of anemia, increasing Hb in anemic patients with LPD and there wasn't found out significant differentiation between all these ESA.

B1648

MANAGEMENT OF STAGE IA DIFFUSE LARGE B CELL NON-HODGKIN'S LYMPHOMA (DLBL): IS RITUXIMAB REALLY NECESSARY?

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Background: Stage IA DLBL is a distinct entity with a favourable prognosis, where a combination of chemotherapy and local radiotherapy afforded durable remissions in the pre-rituximab era. We set out to review our experience of the treatment of this early stage of DLBL.
Aims: To assess the response and relapse rate of stage IA DLBL treated with chemotherapy and local radiotherapy alone, no patient received rituximab in line with national policy.
Methods: We undertook retrospective case notes review of patients treated with radiotherapy alone and those who received both chemotherapy with 3 cycles of cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) and radiotherapy.
Results: Thirty patients were included, treated between 2005 and 2012. The mean age at diagnosis was 78.3yrs (Range 39-95), 23 aged >70yrs. Twenty-seven patients underwent the full course of intended treatment. Of those that did not complete, two discontinued due to intolerance and one declined any therapy prior to commencement. Site of disease frequently involved the head and neck (20 patients), while torso, abdomen and limbs were next most frequent. A greater proportion of deaths occurred in the head and neck group than any other (not all related to lymphoma or treatment). Radiotherapy alone was chosen for 11 patients usually due to frailty, of whom 3 relapsed and 8 died subsequently (2 from lymphoma). Of the combined modality group (16 patients), there were no relapses and three deaths, none lymphoma related. None of these patients received rituximab. Dosage of radiotherapy was 30Gy in ten fractions in 22 patients (3 relapses), while 6 patients received 35Gy (1 relapse) [patient performance status was often poor thus mandating the use of abbreviated fractionation schedules for many]. Two thirds of patients who relapsed after radiotherapy did so within the first 12 months following treatment.
Summary / Conclusion: Radiotherapy alone or chemo/radiotherapy has shown to be effective therapy for patients with stage IA DLBL. Our series show good tolerability of therapy among an elderly group with an acceptable proportion of relapses with radiation alone and none in the combined modality group. It does not appear that rituximab is mandated in this group of patients.

B1649

REARRANGEMENTS OF BCL-2, BCL-6, CYCLIN-D1, IGH, P53 AND C-MYC AS PROGNOSTIC MARKERS IN REPRESENTATIVE TURKISH DIFFUSE LARGE B-CELL LYMPHOMA PATIENTS

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Background: Diffuse large B-cell lymphoma (DLBCL) form a highly heterogenous type with different clinical, morphological, immunological and cytogenetic features, treatment responses, and prognosis. During the last decade, most studies dealing with the heterogeneity of DLBCL have focused on genetic and molecular analyses.
Aims: In this study, we aimed to determine the frequency of BCL-2, BCL-6, CYCLIN-D1, IGH, P53 and C-MYC rearrangements in DLBCL and to assess their prognostic impact.
Methods: A total of 44 patients of DLBCL classified according to WHO classification between 1996 and 2011 were chosen for the study. The samples prepared from the paraffin blocks of lymph nodes were analyzed by fluorescence in situ hybridization (FISH).
Results: Twenty-four of the patients were male and 20 were female and age at diagnosis ranged from 27 to 77 years. Advanced stage (III/IV) was observed in 22 cases (50%). 30 patients (68%) presented with high serum lactic acid dehydrogenase (LDH) levels and 15 patients had high serum B2-microglobulin levels. 28 of the patients with available data had a favourable risk group by the IPI. Succesful FISH analysis was performed in all patients. Rearrangement of BCL-6 was found in 27 patients (61.4%), C-MYC in 14 (31.8 %), P53 in 10 (22.7%), BCL-2 in 8 (18.2 %) and CYCLIN-D1 in 4 (9.1%). Furthermore, 18(41%) of cases showed rearrangements of more than 1 gene. Univariate analysis showed that the IPI score (P=0.013), stage (P=0.025), albumin level (P=0.007) and LDH level (P=0.025) were significantly associated with overall survival Patients with rearrangements of BCL-6 (P=0.053), C-MYC (P=0.483) and P53 (P=0.877) tended to have shorter survival times while patients with rearrangements of BCL-2 (P=0.302) were in a trend for better overall survival.
Summary / Conclusion: The presence of different genetic rearrangements in the same lymphoid tissue samples highlight the complex nature of molecular events in DLBCLs, which is a reflection of the morphologic and clinical heterogeneity of this disease. Our initial results are consistent with the previous literature that showed a different prognostic impact for gene rearrangements. The present study will be extended by including more number of patients with longer follow-up duration.

B1650

PRIMARY BONE LYMPHOMA: CLINICOPATHOLOGICAL CHARACTERISTICS AND TREATMENT RESULTS FROM SINGLE CENTER EXPERIENCE

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for less than 2 percent of all lymphomas in adults, 3 percent of primary bone tumors and 3 to 5 percent of all extranodal non-Hodgkin lymphomas. Men are diagnosed slightly more frequently than women. The vast majority of patients present over the age of 30 years.The radiographic appearances of PBL are variable. Despite this variability, the presence of a solitary, permeative, metadiaphyseal lesion with a layered periosteal reaction on plain radiographs and a soft-tissue mass on MR images, especially in a patient older than 30 years, is highly suggestive of lymphoma. The case for a diagnosis of primary bone lymphoma is further strengthened if the soft-tissue mass and marrow changes are associated with surprisingly little cortical destruction. Histopathologically, the majority of PBL cases have been diffuse large B-cell lymphoma (DLBCL). The patients with PBL treated with combined modality therapy were found to have a superior outcome and a significantly better survival, than the patients treated with single modality therapy.
Aims: To analyze the clinicopathological features of primary bone lymphoma, the role of MR in evaluation of response and correlation between the treatment modality and the outcome.

Methods: Totally 11 patients diagnosed with the primary bone lymphoma, were treated in Institution for radiology and oncology of Serbia in period from 2008.y to 2012.y. The treatment modality, the response and its duration (follow up) were registered for all the patients. We used bone scintigraphy for surveying the entire skeleton and magnetic resonance (MR) imaging to determine the exact extent of local involvement. Whole body CT was performed for each patient in initially staging and in response evaluation of initially pathological findings. MR imaging was used to assess the local outcome of treatment. PET/CT was done for some patients.
Results: Median age of patients was 38 years (range, 27-62). There were 9 male and 2 female patients. Three (27%) patients had B symptoms. Almost all patients were diagnosed with diffuse large B cell lymphomas except one with follicular B cell gradus 3A histology. The most frequent primary site of lymphoma was femur (4 patients). Other primary affected sites were: ossis ilei (3), tibia (2), humerus (1) and thoracic vertebra (1). 91% patients presented with Ann Arbor Stage I or II disease. Regional lymphadenopathy was registered in four patients. 82% patients were treated with combined modality therapy. Eight patients were treated with chemotherapy followed by radiotherapy. One patient was treated by surgery after chemotherapy, due to pathologic fracture. In the combined modality therapy group, the patients received IV to VI cycles of R-CHOP and in the only chemotherapy group, VI to VIII cycles of R-CHOP. Only one patient with high Ki 67 received R-EPOCH regimen. The median follow up was 18 months (range, 6-54). The overall response rate (ORR) for all the PBL patients was 100% as none of the patients showed PD during initial treatment. Seven patients (64%) achieved CR and 4 patients (36%) achieved PR. During response evaluation in all patients, NMR showed disappearing of soft tissue component with persistence of some bone lesions and minimal changes during time. FDG-PET revealed CR in four patients and all patients were alive at the time of the last follow-up and all remain in achieved response.
Summary / Conclusion: Our acquired data demonstrate and confirm that the primary lymphoma involving bone has a good prognosis. But, in our patients, we did not confirm earlier results of protocol influence (combined or single modality therapy) on the outcome. As bone changes that are seen on NMR images are pretty stabile during the treatment period and long time after completion of the treatment, it is difficult to achieve adequate response evaluation using NMR imaging. The need for the further multicenter studies (taking into account the rarity of the disease) in order to define the optimum treatment modality and better response evaluation is emphasized.

B1651
HIV-RELATED HEMATOLOGIC MALIGNANCES PRE-HAART (HIGHLY ACTIVE ANTIRETROVIRAL THERAPY) ERA AND HAART ERA: EXPERIENCE IN ONE CENTRE
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Background: Highly Active Antiretroviral Therapy (HAART) has had a dramatic effect on the natural history of HIV-infected patients. The incidence of AIDS-defining cancers has declined. However, non AIDS-defining cancers have gradually emerged.
Aims: Analyze the clinical and biological features and the outcome of hematologic malignancy among people with HIV infection or AIDS in the era pre-HAART and post-HAART.
Methods: We conducted a retrospective review of HIV-infected patients with hematological malignancies treated in our institution. Pre-HAART era included patients who did not receive HAART.Histological diagnosis was based according to WHO criteria. HAART was defined as a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor along with a backbone of at least two nucleoside reverse transcriptase inhibitors.
Results: Nineteen patients were evaluated, 10 of them belonged to pre-HAART era, and 9 of them belonged to HAAT era. The median age was of 37.3 years, and there was a male predominance. HAART era: the median duration from the diagnosis of HIV infection to development of hematological malignancy was 3 years (range, 0 to 11 years). The histological diagnoses were the following: 3 Hodgkin lymphoma (HL), 5 Non- Hodgkin lymphoma (NHL) and 1 myelodysplastic syndrome. Four of 8 lymphomas had stage II disease and 4 had stage III/IV disease. The 4 patients with stage II disease were concomitantly diagnosed of HIV infection. All patients with advance disease had a previous diagnosis of AIDS, two of them with poor adherence to HAART.
HAART was associated with standard chemotherapy in 8 cases. Five patients died mainly because of chemotherapy-resistant disease. At a median follow-up of 7 months (range, 2 to 48 months), two years progression-free survival (PFS) was 50%. Pre-HAART era: the median time from the diagnosis of HIV infection to development of hematological malignancy was 9 years (range, 2 to 16 years). The histological diagnoses were the following: 3 Hodgkin lymphoma (HL), 7 Non- Hodgkin lymphoma (NHL) and 1 acute myeloid leukemia of intermediate risk. Seven of 10 lymphomas had stage III/IV disease. All of them received standard chemotherapy except one patient with a central nervous system lymphoma. Six patients died: 3 died of lymphoma, 2 patients died after the first cycle of chemotherapy (1 neutropenic sepsis and 1 subdural hemorrhage), and 1 patient died of secondary wasting-HIV syndrome. At a median follow-up of 13 months (range, 1 to 96 months), two years progression-free survival (PFS) was 52%.
Summary / Conclusion: It has decreased the time from HIV-infection diagnosis to hematologic malignancy diagnosis from 9 years to 3 years after HAAR. The reasons for this finding remain unclear. Lymphoproliferative disease was diagnosed at early stage in the HAART era, if the adherence is successfully. Chemotherapy-resistant hematological disease remains the mainly cause of death.

B1652
ONLY RITUXIMAB IN THE EARLY TREATMENT OF INDOLENT LIMPHOMAS RELAPSED AFTER AUTOTRANSPLANTATION
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Background: In the last years the indolent lymphoma has benefited of transplantation procedures.High dose therapy folowed by autotransplantation has been used as salvage or first line tratment for indolent lymphomas.
Aims: The problem is the managment of the relapse of the disease in post-transplant, were as patients higly treated.We reported a single center exsperience in which patients whit indolent lymphomas relapsed after autotransplantatin,were treated only with immunotherapy.
Methods: From january 2005 we have autotransplantated,in our division,23 indolent lymphomas; 15 follicular,7 mantle cells and 1 marginal lymphoma. 13/23 (56%) patients have relapsed by a median PFS of 12 months (range 3-87). All patients received strict follow up with CT and PET and were treated early. 9/13 patients (70%) relapsed (8 follicular,1 mantle cells lymphoma) were treated with 4 weekly doses of rituximab 375 mg/msq for 1 month and then revaluated. If CR have started, maintenance with rituximab 375 mg/msq every 2 months for 2 years. 7/9 patients (80%) revaluated after 4 weekly doses have documented the CR and began rituximab maintenance. All patients who responded had a follicular lymphoma.
Results: With a median follow up of 36 months, 6/7 (85%) patients are in CR and in 4/9 (44%) we have documented grade IV hematologic toxicity (neutrophils<500/mm3) quikly resolved with G-CSF treatment.
Summary / Conclusion: In conclusion, for patients with follicular lymphoma, a strictly follow up may consnent a rapid treatment in relapsed patients after the autologus transplantation and the only immunotherapy may be sufficient to obtain a new CR consolidated by maintenance cycles every 2 months.We need a larger cohort and follow up longer to confirm these data.

B1653
LONGER MEDIAN TIME TO DIAGNOSIS FOR CASES WITH NON HODGKIN LYMPHOMA PRESENTING WITH PLEURAL EFFUSION.
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Background: Non Hodgkin lymphoma presenting with pleural involvement is a rare presentation that is usually confused with other pleural inflammatory and malignant pathologies with consequent diagnostic dilemmas and delay.
Aims: we have thus conducted this retrospective analysis of our non Hodgkin lymphoma database to determine the clinicopathological characteristics of this presentation.
Methods: Non Hodgkin lymphoma (NHL) patients treated at Cairo Oncology Centre (Cairo, Egypt) in the period from 2000-2008 were reviewed. Eligible patients were those who had complete information on date of diagnosis, histopathological and immunohistochemical confirmation of the diagnosis. We compared the difference in clinicopathological parameters between cases presenting with and without pleural involvement.
Results: In the period from 2000-2008; 380 Non Hodgkin lymphoma patients were included in the analysis fulfilling the inclusion criteria. Of which 26 patients only have definite radiological evidence of pleural involvement (6.8%). Pleura was the only site of disease in 2 cases, associated with nodal involvement in 16 cases and associated with both nodal and extranodal localization in 8 cases (of which 3 cases have pulmonary parenchymal involvement).of the nodal sites involved with the pleura, mediastinal nodes were involved in 13 cases. DLBCL was the diagnosis in 18 cases (69%), small lymphocytic lymphoma in 5 cases and follicular, Mantle cell and anaplastic T cell lymphoma one case each. Cases with pleural involvement were more likely to have higher LDH (P=0.005) and aggressive histology (0.05). Median time from initial presentation to established diagnosis is 2 months; pleural fluid aspirate was used in 10 cases; of which 6 cases needed further confirmation by a tissue biopsy.
Summary / Conclusion: According to our data, patients with NHL presenting with pleural involvement have a longer time to diagnosis with more diagnostic dilemmas, FNA from the pleural fluid should not be routinely considered as the diagnostic procedure of choice for cases with suspected NHL but rather tissue biopsy from accessible sites should be the standard.

B1654

BLASTIC PLASMOCYTOID DENDRITIC CELL NEOPLASM (BPDCN): SINGLE CENTER EXPERIENCE WITH TWO CASES IN ONE YEAR

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Background: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, highly aggressive hematopoietic malignancy that is characterized by cutaneous infiltration with or without bone marrow involvement and further leukemic spread. Its overall incidence is very low, accounting for 0.44% of all hematologic malignancies. The leukemic form of the disease is an extremely rare situation, representing <1% of all cases of acute leukemia. BPDCN predominantly affects males, with a sex ratio of 3:1, and generally occurs in the elderly.
Aims: The aim of this presentation was to evaluate symptoms, signs and outcome of two cases of BPDCN.
Methods: Between February 2012 and January 2013, we identified 2 patients with BPDCN presenting with skin lesions. Data regarding clinical presentation, diagnosis, staging, treatment and outcome was collected.
Results: First patient was female, 78 years-old, the other one was male, 75 years-old. At diagnosis both had asymptomatic skin lesions. The female patient presented with a cutaneous lesion on her right shoulder since the last month. Laboratory data disclosed anemia (hemoglobin: 11, 3 g/dl) thrombocytopenia (139×10^9/L) and morphologically immature atypical cells in the peripheral blood. Bone marrow aspiration showed 5% infiltration of immature blastic cells with the following immunophenotype: CD45(+), CD123(+), CD85k(+), CD33(-), CD14(-), CD16(-), CD19(-), CD5(-), CD10(-), CD20(-)CD56(+)20%, CD4(+), NG2(+). No chromosomal alterations were detected by cytogenetic analysis of the bone marrow. She had axillary, jugular, submandibular, and supraclavicular lymphadenopathy. Cutaneous, lymph node and bone marrow biopsies, all confirmed the diagnosis of BPDCN. She was treated with Cy-VAD (cyclophosphamide, vincristine, adriamycin and dexamethasone). She achieved CR, continued with induction 2 chemotherapy with Vepesid-Aracytin and died 4 months later of multi-organ failure. The male patient had a generalized purplish dermal rash arising from the head to the lower extremities that presented one week before and progressed very rapidly. Laboratory data revealed anemia (hemoglobin: 10, 9 g/dl), thrombocytopenia (100×10^9/L), WBC: $8.30*10^3$/µL with 42% of morphologically immature atypical cells. Bone marrow aspiration showed 88% infiltration of immature blastic cells with the following immunophenotype: CD45 (+) low, CD43 (+), CD123 (+), CD56 (+), CD4(+), CD34 (-).Cytogenetic analysis showed deletion of the long arm of chromosome 12 - deletion of ETV6 gene and deletion of the long arm of chromosome 17- deletion of P53 gene. Computed tomography scans did not disclosed any pathologic lymphadenopathy. Histopathology of skin lesions showed infiltration of blastic cells. Immunohistochemical analysis confirmed the presence of cells with the same immunophenotypic features. He started chemotherapy with Zavedos and Aracytin (3+7) and he is now in CR after this induction.
Summary / Conclusion: We present two cases of a rare clinical entity with cutaneous and bone marrow infiltration with blastic plasmocytoid dendritic cells. The diagnosis relied on the immunophenotypic features of the malignant cells, particularly with the presence of CD4 (+) and CD 56(+). Several treatment options have been used so far, all with poor results. The ALL-type treatment regimen that seems to result to a better outcome according to a recent publication resulted to a very short survival. Unfortunately neither of them could proceed to bone marrow transplantation, which is a better therapeutic option for younger patients with good performance status.

B1655

IMMUNOCHEMOTHERAPY-INDUCED CARDIOVASCULAR COMPLICATIONS IN PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA: RESPONSE TO ZOFENOPRIL

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Background: The aim of this study was to determine the protective effect of zofenopril in immunochemotherapy-induced cardiomyopathy. The natural history of immunochemotherapy-induced cardiomyopathy, as well as its response to cardiovascular therapy, remains poorly defined. Hence, evidence-based recommendations for management of this form of cardiomyopathy are still lacking. Zofenopril proved to be effective in patients with coronary artery disease and myocardial infarction, thanks to its unique effective mechanism of action for improving blood pressure control, left ventricular function and myocardial ischemia burden, as well as angiotensin-converting enzyme inhibition. Rituximab is a monoclonal antibody to CD20 that has activity in leukemia and lymphoma.
Aims: This study aims to describe the complications and outcomes of a subset of patients with diffuse large B-cell lymphoma who were treated with immunochemotherapy.
Methods: Patients with diffuse large B-cell lymphoma in whom rituxmab, doxorubicin, cyclophosphamide, vincristine, and prednisolone therapy was planned were enrolled in the study. We included in the study 14 patients in zofenopril and 10 patients in control groups. In the zofenopril group, 7.5 mg twice-daily oral zofenopril was given during 3 months. The patients were evaluated with echocardiography before and after chemotherapy. Left ventricular ejection fraction (EF) and systolic and diastolic diameters were calculated.
Results: At the end of 3 months of follow-up, 1 patient in the zofenopril group and 2 in the control group had died. Control EF was below 50% in 2 patient in the zofenopril group and in 3 in the control group. The mean EF of the zofenopril group was similar at baseline and control echocardiography (64.6 vs. 64.8, respectively; P=0.2), in the control group the mean EF at control echocardiography was significantly lower (62.7 vs. 49.2; P<0.001). Both systolic and diastolic diameters were significantly increased compared with basal measures in the control group. In Doppler study, whereas E velocities in the zofenopril group decreased, E velocities and E/A ratios were significantly reduced in the control group.
Summary / Conclusion: Prophylactic use of zofenopril in patients with diffuse large B-cell lymphoma receiving immunochemotherapy may protect both systolic and diastolic functions of the left ventricle.

B1656

A RARE CAUSE OF GENERALIZED LYMPHADENOPATHY: ROSAI DORFMAN DISEASE

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Background: Rosai Dorfman Disease is a rare benign disease characterized by generalized lymphadenopathies usually involving cervical lymph nodes. Its association has been reported with other autoimmune conditions and malignancies at the time of diagnosis or during its course. Anemia, polyclonal gammapathy and high sedimentation rate are remarkable findings in the laboratory investigations. Diagnosis is made by biopsy of the involved lymph node. Although the condition is a benign entity presenting with spontaneous remissions, it also may be lethal in the case with multi organ involvement associated with other autoimmune conditions.
Aims: We present here four cases followed in our center with diagnosis of Rosai Dorfman Syndrome.
Results: All of the cases presenting to our center with cervical lymphadenopathy were male and their median age was 49 years (range: 41 – 80 years). Anemia compatible with anemia of chronic diseases was found in all cases at the time of presentation. In regard to laboratory investigations, all cases had high levels of globulin, C-reactive protein and high rate of sedimentation, and polyclonal gammopathy.Diagnoses of all patients were made with biopsy of lymphadenopathy.In regard to follow-up of the patients, anemia worsened and increased level of creatinine was found after follow-up of 4 years without treatment. Biopsy results of the patient for whom renal biopsy was performed because of suspicion of renal involvement is still being waited, and steroid treatment was scheduled to the patient after the result of the biopsy. Hodgkin lymphoma developed in the course of one patient. Complete remission occurred with 4 courses of ABVD chemotherapy.New mass lesion was found in lung parenchyma on imaging studies following 6th course of ABVD chemotherapy.This patient whose result of lung biopsy has come as pulmonary adenocarcinoma is still receiving chemotherapy in the oncology unit for lung cancer. Steroid treatment was given to two patients with complaints of fever, weight loss, fatigue due to anemia (hemoglobin level was 8 g/dL and 6 g/dL, respectively). Fever response occurred with steroid treatment in both patients and their symptoms were controlled. High rate of sedimentation and high level of globulin normalized in the patients with anemia resolved. In one patient receiving steroid treatment, chronic renal failure developed due to accompanying cresenteric glomerulonephritis. The patient is still on chronic hemodialysis program. Steroid treatment is still continuing in both patients.
Summary / Conclusion: Although Rosai Dorfman syndrome is rare, lymphadenopathy should be kept in mind in differential diagnosis. It should be remembered that although it is a benign condition, it may be associated with other autoimmune conditions or malignancies at the time of diagnosis or during its course, and that it should be treated for symptoms due to such associated conditions and the patients should be followed for this.

B1657

POSITRON EMISSION TOMOGRAPHY SCAN FOR FOLLICULAR LYMPHOMA: GOOD CORRELATION WITH CLINICAL AND HISTOLOGIC FEATURES AT DIAGNOSIS

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Background: To date, positron emission tomography (PET) scan is not the standard in the staging at diagnosis of follicular lymphoma. Its use is limited to those cases in which residual disease is crucial for therapeutic decisions and only if transformation to a high-grade lymphoma is suspected.
Aims: Our aim is to demonstrate a positive correlation between the standardized uptake value (SUV) at biopsy site detected by PET scan with pathologic (Ki67 and follicular lymphoma histologic grade) and clinical (LDH, beta-2-

microglobulin, Ann Arbor stage and Follicular Lymphoma International Prognostic Index -FLIPI) features at diagnosis.
Methods: We retrospectively detected in the last 3 years 10 patients in whom node biopsies were performed taking into account the maximal SUV detected in the PET scan at diagnosis. The statistical analysis was made with SPSS version 20 for MAC-OS; descriptives and one-tailed Pearson's correlation test were calculated.
Results: The mean at diagnosis for SUV at biopsy site was 9.29 (range 4-24), for LDH the mean was198.90 U/L (range 135-290), for beta-2-microglobulin 3 mg/L (range 2-6) and for Ki67% index was 22% (range 5-50%).
Three (30%) patients had a histologic grade1, 6 (60%) cases were grade 2 and 1 patient (10%) was grade 3a. Six cases (60%) were stage IV of Ann Arbor, 3 (30%) were stage III and 1 (10%) case was stage II. The one-tailed Pearson's correlation test showed correlation (r>0) of SUV at biopsy site with beta-2-microglobulin (r=0.667; P<0.05), FLIPI (r=0.744; P<0.05), histologic grade (r=0.797; P<0.05) and Ki67 (r=0.885; P<0,05). We did not find correlation with serum LDH (r=0.120; P=0.37).
Summary / Conclusion: The SUV measured in the PET scan at biopsy site correlates with almost all the daily used pathologic and clinical parameters. The serum lactate dehydrogenase (LDH) is not frequently elevated in low-grade lymphoma, this may be the reason why no correlation was found. The most clinically important correlation detected with SUV is the histologic grade.(figure 1). The follicular lymphoma histologic grade has a prognostic value and also a therapeutic implication. The Pearson's r=0.8 reveals a lineal dependence between both variables. In practice, the computed tomography scan is used for the staging of follicular lymphoma but with this radiologic technique it is impossible to detect which lymph nodes have a higher histologic grade. Many patients are misdiagnosed as follicular lymphoma when in fact they already have a high-grade lymphoma. With this little approach we will consider using prospectively PET scan as guidance for node biopsy at diagnosis and make a new statistical analysis with a higher number of patients.The SUV measured in the PET scan at biopsy site correlates with almost all the daily used pathologic and clinical parameters. The serum lactate dehydrogenase (LDH) is not frequently elevated in low-grade lymphoma, this may be the reason why no correlation was found. The most clinically important correlation

B1658
ERDHEIM-CHESTER DISEASE PRESENTED WITH CENTRAL NERVOUS SYSTEM INVOLVEMENT: A CASE REPORT
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Background: Erdheim–Chester disease (ECD) is non-Langerhans form of histiocytosis of unknown origin. It is rare disease. The clinical picture may vary from asymptomatic bone lesions to multisystemic and life-threatening forms with poor prognosis, especially in case of specific central nervous system (CNS) or cardiovascular involvements .It is mainly diagnosed by typical pathologic features with the biopsy specimen displaying the xanthomatous or xanthogranulomatous infiltration of tissues by $CD68^+$ $CD1a^-$ S-100± spumous histiocytes, which distinguished from Langerhans cell histiocytosis. Although steroids has been the most common medical treatment in this disease an optimal therapeutic strategy remains to be defined. Interferon α-2a (IFN-a) has recently demonstrated valuable results in ECD, specisificly with CNS involvement.
Aims: Herein, we present a 35–year-old patient with ECD who had intra cerebral tumor-like lesion, which have occasionally been reported.
Results: A previously healthy 35–year-old woman, except visual impairment in left eye due to cataract for last 2 years, presented to the neurology department with complaints of weakness and headache 5 months ago. Headache was throbbing type on temporofrontal region and last in 5 minutes. Any pathological sign was found on physical examination. Cranial magnetic resonance imaging (MRI) revealed a 3x3.5 cm mass on the level of left basal ganglion, which was heterogenic contrasted on central part. Due to edema and mass, 3. Ventricular and the left frontal horn of lateral ventricular were compressed. Dekzamethazon treatment was initiated. The patient was referred to neurosurgery department for biopsy from that mass. The biopsy revealed infiltration of CD 68^+ S 100^+ $CD1a^-$ non-Langerhans histiocytes which were consistent with ECD. The patient was referred to our department. The physical examination of the patient was normal. Although deksamethazon dose was lowered the patient was still receiving it about one month. Laboratory studies revealed an elevated C-reactive protein (>4.4 mg/L) and erythrocyte sedimentation rate (45 mm/hour), and decreased hemoglobin level (10.1 g/dl) which was compatible with iron deficiency anemia. The other laboratory studies including urea and electrolytes, lipids, urinary studies, liver function and antinuclear antibodies were all within normal limits. Radiologic studies including direct x ray and 99Technetium (Tc) scintigraphy of long bones, thoracal and abdominal computed tomographics and heart echocardiography were normal. Dexamethazon was stopped and 3 million units in 3 days for a week interferon α-2a and oral iron treatments were started. Interferon treatment was well tolerated. There was a marked regression on cranial MRI scan after 3 months. The mass was almost completely disappeared and the impression of the mass and edema were not seen.
Summary / Conclusion: As a result, IFN-a was a very effective treatment in our ECD patient with cranial mass, which is rarely seen.