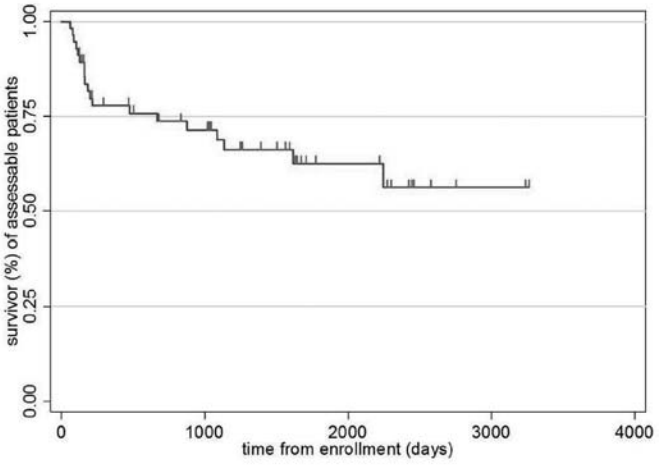
Radiation and surgery were used when indicated. Eleven patients died early, before any treatment was completed (median time 18 days, range 5-56); 2/69 patients were lost at follow-up. Therefore, a total of 56 patients underwent their scheduled treatment and were evaluable for the outcome. We observed 10/56 deaths because of treatment related toxicity or disease progression. Complete remission (CR) was achieved in 45/56 (80%) patients. Of these, 8 (18%) relapsed, mostly responsive to second line therapy (7/8 patients), and 10 patients died because of late treatment-related toxicity or infection. One patient is still alive in partial remission (PR) at 23 months. The median survival time of evaluable patients was not reached at 3250 days (see Figure 1). *Conclusions*. We can confirm that PTLD is a significant cause of mortality in solid organ transplant recipients: in our study the overall mortality rate was 45% (31/69) and the exitus mostly represents an early event, occurring within 6 months from diagnosis in 20/31 patients (64%). Nevertheless, timely and tailored treatment of the disease and its complications warrants long-lasting complete response with low relapse rate. PTLDs are characterized by wide clinico-pathological variability and represent a heterogeneous disease: better knowledge of biological parameters (e.g. EBV pathogenic role, donor or recipient PTLD origin, immunologic status of patients) could help to stratify our patients in different risk groups and could allow more appropriate treatment.



0213

RISK OF SECOND CANCER IN NON-GASTRIC MARGINAL ZONE B-CELL LYMPHOMA OF MALT: A POPULATION-BASED STUDY FROM NORTHERN ITALY

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Background. Marginal zone B-cell lymphomas (MZL) of MALT show a peculiar relationship with the triad autoimmunity-infection-immunosuppression. For this reason, these lymphomas have been studied for the risk of second cancers. Most series reported so far regard patients with gastric MALToma, while data on nongastric MZL of MALT are lacking. *Aim.* To define the risk of second cancer in nongastric MZL of MALT in a population-based study from Northern Italy. *Methods.* We studied the prevalence of second cancers in a series of 157 patients with nongastric MZL of MALT consecutively diagnosed in two haematological Institutions of the Northern Italy region Lombardia. We compared the occurrence of second cancer with respect to the general population by calculating the standardized incidence ratio (SIR), with the age- and sex-specific incidence rates of the Cancer Registry of Lombardia as a reference. *Results.* A history of 30 additional neoplasms was documented in 29 patients (18%) (18 females and 11 males): 21 previous, 3 concurrent, and 6 subsequent. The malignancies were: 25 solid tumors, 2 hematological diseases (1 Hodgkin's lymphoma and 1 essential thrombocythemia), 3 non-melanoma *in situ* skin cancers. One patient had two malignancies (breast cancer and essential thrombocythemia), both prior to the diagnosis of cutaneous lymphoma. The sites of solid cancers were: 8 breast, 4 endometrium, 4 skin, 3 thyroid, 2 lung, 1 prostate, 1 colon, 1 small intestine, 1 salivary gland, 1 bladder, 1 ovary and 1 stomach. In 4 patients the site of cancer and lymphoma was the same. For the entire group, the SIR of an additional malignancy was 0.8 (95% CI: 0.55-1.17, p=0.2). The relative rate of an additional malignancy was 0.7 for males (95% CI: 0.39-1.26, p=0.2) and 0.89 for females (95% CI: 0.55-1.46, p=0.6). The comparison of risks between males and females was not significant (SIR ratio 1.28, 95% CI: 0.59-2.76, p=0.5). After excluding non-melanoma skin cancers, the SIR of a second tumor was 0.75 (95% CI: 0.5-1.12, p=0.2). The relative rate of a second tumor was 0.6 for males (95% CI: 0.31-1.15, p=0.1) and 0.89 for females (95% CI: 0.54-1.47, p=0.6). The comparison of risks between males and females was not significant (SIR ratio 1.49, 95% CI: 0.65-3.4, p=0.3). After excluding all previous malignancies, the SIR of a second cancer was 1.32 (95% CI: 0.69-2.55, p=0.4). All concomitant and subsequent malignancies were invasive tumors. The relative rate of a second cancer was 1.46 for males (95% CI: 0.61-3.51, p=0.4) and 1.19 for females (95% CI: 0.44-3.16, p=0.7). The comparison of risks between males and females was not significant (SIR ratio 0.81, 95% CI: 0.22-3.02, p=0.8). *Conclusions.* These data demonstrate that patients with nongastric MZL of MALT are not at increased risk for second cancer compared to the general population of the same geographical area. However, since nongastric MALT lymphoma is a long-lasting disease of advanced age with high risk of relapse, a careful clinical follow up is always warranted.

0214

ACHIEVEMENT OF MOLECULAR REMISSION AFTER FIRST LINE TREATMENT PROLONGS SURVIVAL IN FOLLICULAR LYMPHOMA PATIENTS

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Backround. However is follicular lymphoma (FL) still considered conventionally incurable disease, prolonged complete remissions were reported. Results of recent studies suggest, that patients who achieve complete remission (CR) with PCR bcl-2/IgH negativity (molecular remission, CRm) have better long term outcome. *Aims.* To evaluate whether achieving of molecular remission after first line treatment have an impact on disease free (DFS) and overall (OS) survival in all risk subgroups, previously untreated, follicular lymphoma patients. *Methods.* 104 (pts) with FL were diagnosed and treated in our department during last 8 years. All of them were examined with a qualitative PCR (bcl-2/IgH) from bone marrow (BM). Bcl-2/IgH (MBR, mcr or long-distance PCR) positivity was observed in 55 pts (57%) at the time of diagnosis. 91% of bcl-2/IgH+ pts had an advanced disease stage (III/IV), BM involvement was present in 43.5% bcl-2/IgH+ pts. First line treatment was stratified acording generally used risk factors (FLIPI, GELF, β-2-m level, bulk disease). Patients under 60 (65) y.o. with high risk disease (FLIPI ≥3 or additional risk factors) were indicated to stem cell transplantation (SCT). 19 patients underwent autologous and 1 patient allogenic SCT. 36 patients were treated conventionally (CHOP or fludarabine based regimens). Rituximab was administred as first line concomitant chemo-immunotherapy in 21 pts (equally in both groups). PCR (BM and/or peripheral blood) was reevaluated on the day +100 after SCT or at the point of restaging and during follow-up every 6 months.

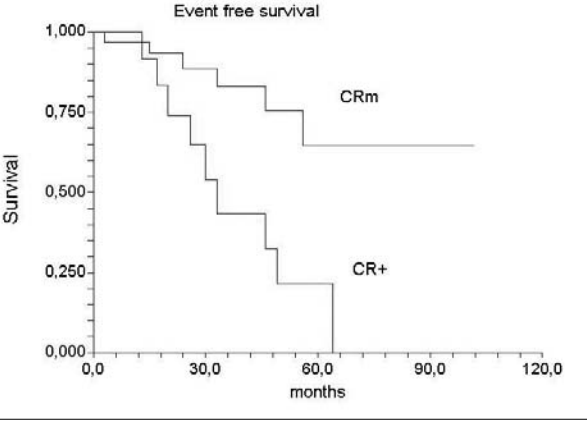

Figure 1. Event free survival: impact of residual disease.

Results. After first line treatment 35/55 (64%) pts achieved CRm, 13 pts (24%) CR+, 9 (16%) PR+ (partial response). After SCT (81.8%) pts attained CRm (100% receiving rituximab in the 1st line). Median follow up is 50 months (mo). 23/55 (41.8%) pts relapsed or progressed (median PFS 30 mo), 11 pts died - one in CRm due to acute graft versus host disease, the other due to progression of the disease. At present 32/35 CRm pts are still in CRm, whereas 6/11 pts in CR+ relapsed. Median disease free survival (DFS) was longer in CRm pts than in CR+ pts (median EFS 33 mo vs not reached, p 0.0024). Median DFS in patients with or without autologous stem cell transplantation was not significantly different. Patients in CRm have longer overall survival (64 mo vs not reached, p 0.05) compared to pts in CR+ and PR. *Summary.* Molecular remission after first line treatment have an impact on disease free and overall survival in all risk subgroups of FL patients. Persistent PCR bcl-2/IgH positivity is asociated with high risk of relapse and additonal (maintenance) treatment should be considered.

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0215

CLINICO-BIOLOGICAL CHARACTERISTICS OF PATIENTS WITH DIFFUSE LARGE B CELL LYMPHOMA AND HEPATITIS C VIRUS INFECTION

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Background. The infection with Hepatitis C Virus (HCV) is involved in the etiology of some subtypes of non Hodgkin's lymphoma (NHL) as diffuse large B cell lymphoma (DLBCL). *Aims.* We tried to analyze the clinico-biological characteristics of a group of 82 patients with DLBCL associated with HCV infection. *Methods.* We did a retrospective analysis of the clinical and biological profile of 82 patients hospitalized in the Hematology Clinic during 1993-2003. All patients were HIV negative and they were positive at diagnosis for the HCV antibodies Elisa method. The statistical analysis was performed with the special programs EPI INFO 6 and INSTAT. *Results.* The characteristics of the diffuse large cell lymphoma group that we studied were: medium age - 52,2 years; males/females=1/1; extranodal determinations - 48 cases (58.5%)- primitive extranodal 25 cases (30.5%) and secondary extranodal 23 cases (28%); B signs - 66 patients (80,5%); IK < 70 - 40 cases (48,8%); IPI at diagnosis was 16% low, 24% int.low, 35% int/high and 25% high; Bulky disease - 35 cases (42,7%); clinical stage I, II/III, IV=40/41; medullar determination - 14 cases (17,2%); LDH = 672,024±598,128 U/l; ESR = 50,45±37,73 mm/h; Ki67 = 51,90±22,16. The transformation from a low grade lymphoma in a DLBCL was 10% and primary mediastinal DLBCLwas 5%. The most important extranodal determinations were the stomach, the spleen, the liver, the skin. The treatment was CHOP or CHOP-like regiments. A small number of cases received CHOP and Rituximab. 11% of patients with severe liver dysfunction received monochemotherapy or radiotherapy only. In 5% of DLBCL and HCV positive patients the chemotherapy was discontinuous because of the hepatic failure. Medium follow-up was 48 month for the survivors and the overall survival at 5 years was 59%, while failure free survival at 5 years was 34%. *Conclusions.* It is important to recognize the clinical and biological features of DLBCL with HCV positive patients for bigger groups, which could clarify the connection between HCV infection and aggressive non Hodgkin lymphomas. It is also necessary to continue the study in order to evaluate the differentiate survival of nodal and extranodal types of lymphomas.

0216

RITUXIMAB IN INDUCTION TREATMENT AND IN HIGH DOSE CHEMOTHERAPY PRIOR TO AUTOLOGOUS STEM CELL TRANSPLANTATION AS FIRST LINE THERAPY IN STAGE III-IV DIFFUSE LARGE B-CELL LYMPHOMA AT POOR PROGNOSIS

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Background. We investigated efficacy and safety of adding Rituximab (R) to induction and intensified HDC as part of first line treatment in pts with aa-IPI at Intermediate-High (IH) or High (H) risk with B-DLCL at diagnosis, comparing two groups of pts enrolled in two non-randomized phase II clinical trials with up-front HDC and ASCT with or without R. Aims and *Methods.* 118 previously untreated pts <61 years with B-DLCL, stage III-IV at aa-IPI IH or H risk were treated: 41 pts were enrolled into HDC trial (control group; August 1991-August 1995) and 77 pts into R-HDC trial (study group; January 2001-December 2004). Treatment in R-HDC study group consisted in an induction treatment lasting two months with four courses of R-MegaCEOP chemotherapy (R 375 mg/m^2 day1, CTX 1200 mg/m^2 + EPI 110 mg/m^2 + VCR 1.4 mg/m^2 day3 and PDN 40 mg/m^2 days3-7) every 14 days with G-CSF support; then two courses of intensified chemoimmunotherapy R-MAD (Mitoxantrone 8 mg/m^2 + ARAC 2000 mg/m^2 /12h + Dexamethasone 4 mg/m^2 /12h for 3 days and R 375 mg/m^2 day4 and before PBSC harvest) followed by ASCT with BEAM as conditioning regimen. Treatment in HDC control group was an induction treatment lasting two months with MACOPB x 8 weekly infusions followed by the same intensified and HDC regimens (MAD x 2 courses + BEAM and ASCT). IF RT was given to areas of previous bulky disease in both trials. *Results.* Pts characteristics in both trials were comparable with no statistically significant differences: median age was 45 years (19-60); 51% were at H risk; 36% had bone marrow (BM) involvement, 80% LDH>normal and 42% extranodal sites>1. Complete Response at the end of the treatment was: 60 pts (78%) in R-HDC group and 28 (68%) in HDC group (p=.25). Failures (17% vs 25%) and toxic deaths (5% vs 7%) were comparable between the two groups (R-HDC vs HDC). Short-term toxicity appeared similar. NO MDS or ANLL or solid tumours were reported in both arms. No differences were observed in neutrophils >500/mm^3 and platelets >50000/mm^3 engraftment; median times in R-HDC vs HDC were: 9 vs 10 and 15 vs 16 days. Median follow-up was 36 months in study group and 72 months in control group. Three-year failure-free survival (FFS) and 3-yr overall survival (OS) rates in R-HDC group vs HDC group were: FFS 64% vs 46% (p=.016); OS 80% vs 54% (p=.004). A better outcome for pts treated with R-HDC was confirmed in both IPI groups (IH and H risk). A Cox's model was performed to adjust the effect of treatment for competing risk factors (age, IPI, BM involvement, number of extranodal sites). In this multivariate analysis the risk of failure and death was confirmed as significantly reduced in R-HDC group: adjusted hazard ratio (R-HDC vs HDC) was 0.56 (95% CI=0.30-1.01, p=.05) for FFS and 0.42 (95% CI=0.21-0.88, p=.02) for OS. *Conclusions.* these results suggest that the addition of Rituximab to induction and intensified chemotherapy before BEAM and ASCT is effective and safe in B-DLCL at poor prognosis.

0217

EFFECTS OF PRE-TRANSPLANTATION TREATMENT WITH RITUXIMAB ON OUTCOMES OF AUTOLOGOUS STEM-CELL TRANSPLANTATION FOR DIFFUSE LARGE B-CELL LYMPHOMA

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Background. Rituximab (R) in combination with chemotherapy (CHT) has become standard treatment for patients (pts) with diffuse large B-cell lymphoma (DLBCL). However, there are limited data concerning the comparison of the use of R-CHT and CHT alone before high-dose therapy (HDT) either as a part of induction regimen or as a part of salvage treatment. *Aims.* We retrospectively analysed the efficacy of R-CHT versus CHT without R followed by HDT and autologous stem cell transplantation (ASCT) in patients with DLBCL. *Methods.* Out of 127 pts with DLBCL who underwent HDT with ASCT, 59 pts received R as part of chemotherapy regimen (R-CHT group): 32/59 (54%) received HDT in 1st CR. 68 pts received CHT without R (CHT group): 14/68 (21%) received HDT in 1st CR (p<0.0001). Patient characteristics were comparable in both groups with the exception of status at HDT, indi-