extranodal lymphoma

478 PRIMARY EXTRANODAL NON HODGKIN'S LYMPHOMA (NHL): PRESENTATION OF 463 CASES FROM TWO ONCOLOGIC CENTRES IN BUENOS AIRES ARGENTINA: MARIE CURIE HOSPITAL AND HENRY MOORE INSTITUTE. 1997-2007.

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Introduction: Out of a total of 1260 cases of LNH registered at M. Curie Hospital and H. Moore Inst. in Bs As, 563 cases with extranodal localization were reported. This account for 36,74% of the total number. All patients undergo staging procedures, included CT scan of thorax, abdomen, pelvis and bone marrow biopsy. Primary extranodal lymphomas are still a controversial topic. Nodal localizations like the involvement of Waldeyer's ring, spleen and thymus are included in reports as well as diseminate disease at nodal and extranodal sites. According Ann Arbor, we take into account patients with IE and IIE stage.

Material and methods: Population mostly, residents of Bs As and its surroundings. To a lesser extent, from the interior of the country or neighbouring countries.

Results: Distribution according to sex: males 52.05%, females 47.95%. Range of ages: 17-90 years. Average age: 56.42 years. B progeny: 406 (87.7%), T progeny: 57 (12.3%). The histologic subtypes are classified as: high grade 190 (41.04%), low grade 158 (34.12%), unclassified 115 (24.83%). 24 cases (5.18%) of HIV positive were recorded, high grade 21 and low grade 3. In the high grade there were 6 of plasmablastic lymphoma, 5 of the oral cavity and 1 of the ovary. Distribution according to localization: Skin 68, Tonsil 54, Orbital 46, Oral cavity 38, Soft tissues 35, Stomach 33, Bone 32, Bowels 23, Breast 18, Parotid 18, Brain 14,Paranasal sinuses 12, Cavum 11, Oropharinx 10, testicle 9, Lung 8, Scalp 5, Salivary glands (other than parotid) 5, Spinal cord 4, Spleen 3, liver 3, rectum 3, larinx 2, ovary 2, thyroid 2, uterus 2, choroid membrane 1, perineum 1, pleura 1.

Conclusion: An analysis of the variables: age, sex, histology, localization and HIV is presented. The percentage of extranodal NHL (36.74%) is in keeping with that of international records. The predominance of certain localizations, less frequent in other records, is due to the selective referals of head and neck and ofthalmologic oncologic pathologies to M. Curie Hospital.

479 A PHASE II STUDY OF BORTEZOMIB IN PATIENTS WITH MALT LYMPHOMA

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Introduction: The proteasome inhibitor bortezomib has demonstrated activity in a wide spectrum of lymphoid malignancies, but has not been tested in patients with MALT-lymphoma. In view of this, we have initiated a phase II study in order to assess the activity and toxicity of bortezomib in patients with MALT-lymphoma.

Patients and Methods: 16 patients with histologically verified MALT lymphoma were enrolled in the trial. Four patients had gastric MALT-lymphoma, 7 of the ocular adnexa, one of the colon, and 2 of the parotid, and one patient each suffered from MALT-lymphoma of the lung and the breast. Treatment consisted of bortezomib at a starting dose of 1.5 mg/m^2 on days 1, 4, 8 and 11 repeated every 21 days. After 4 cycles of therapy, restaging was performed, and patients with response to treatment or stable disease continued treatment for another 4 cycles.

Results: Currently, 15 patients are evaluable for response and 16 for toxicity. The overall response rate was 75% (12/15 evaluable patients) with 8 achieving complete remission (53%) and 4 having partial response, while 3 patients had stable disease. After a median follow-up time of 20 months (range; 4–24), all patients are alive. Four patients have relapsed, while the remaining 12 continue to be in remission. A median of 8 cycles were given per patient (range; 4–8), with 2 patients discontinuing treatment after four courses. All patients except one, however, required consecutive dose reductions due to either neuropathy (7 patients) or diarrhea (8 patients).

Conclusion: Judging from our data, boretzomib appears to be active in patients with MALT-lymphoma. However, a high rate of toxicities was seen in our cohort of patients due to the high intial dose, warranting further assessment of combination schedules with bortezomib at lower doses than given in our study.

480 RITUXIMAB+MACOP-B (R+MACOP-B) AND RADIOTHERAPY IN PRIMARY MEDIASTINAL LARGE B CELL LYMPHOMA: A SINGLE INSTITUTION EXPERIENCE

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Introduction: Primary mediastinal (thymic) large B-cell lymphoma (PMLBCL) is recognized as a separate subtype of diffuse large B-cell lymphoma with unique clinical and immunopathologic characteristics and relatively favorable outcome. The standard of care this type of lymphoma not yet well established. The aim of our study was to evaluate the efficacy and safety of R±MACOP-B regimen followed by radiotherapy (IFRT) in PMLBCL.

Methods: Between 2004 and 2007, 21 previously untreated patients (pts) with PMLBCL were diagnosed and treated at our center. The median age was 28 years (range 18-47) and 12/9 (57%) were females; 12 pts had stage II and 9 stage IV; 19 (91%) presented a bulky disease and 7 (33%) had a superior vena cava syndrome; 14 (66%) had B symptoms, LDH was increased in 15 (72%) pts. According to the age-adjusted IPI score 9 pts (43%) had IPI=0-1 and 12 pts (57%)=2-3. The most frequent involved extranodal site was lung 12 (57%), 8 (38%) pts had pleural and 6 (29%) pericardial effusions. All patients were treated with standard MACOP-B regimen, 10 pts received Rituximab (375 mgm^2 – N 4-6). Mediastinal IFRT at dose 30-36 Gy was given to 16 (76%) patients.

Results: The response rate at the completion of the programme was CR/CRu=18 (85%), PR=2 (10%) and NR=1 (5%); 6 patients obtained a CR/CRu following IFRT. After a median follow up 16 months, the 2-years PFS and OS were 84% and 94% respectively. During the treatment 15 pts had different infectious and toxic complications: stomatitis – 8, pulmonitis – 3, hepatitis – 2, pneumonia – 6. These complications resulted in interruption of treatment of 6 pts, one patient died from pulmonary aspergillosis.

Conclusions: Our data confirms that R±MACOP-B followed by IFRT are highly effective therapeutic regimens for patients with PMLBCL; however one should be cautioned about the significant complications. Small number of pts does not allow us to link the toxicity with use of Rituximab. Futher studies are needed to finally define value of R±MACOP-B and its superiority over R-CHOP.

481 LOW GRADE B - CELL BRONCHIAL ASSOCIATED LYMPHOID TISSUE (BALT) LYMPHOMA THAT SIMULATE A LUNG'S LOCALIZATION OF HODGKIN'S LYMPHOMA

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Introduction: We describe the case of a man who was diagnosed a BALT after the RC of Hodgkin lymphoma. The combination of a BALT with Hodgkin's lymphoma is exceptional.

Materials and Methods: A 62 years old patient was undergo to a cervical node biopsy that depose for a sarcoidosis and started therapy with prednisone without improvement. One year ago, for the progression of disease, the patient was undergoes a new node biopsyoflater cervical site and tonsil left that conclude with lymphoma of Hodgkin, nodular sclerosis. The staging was IVAE for the lung's lesions-PET positive and a localization at tonsil left. ABVD chemotherapy was started and after two cycles early-Pet was negative. After six cycles he was in RC - PET negative. After three months from the end of chemotherapy, for cough and dyspnoea, the patient was subjected to pulmonary tomography that documented consolidate areas, PET positive, of the lung. A lung's biopsy make the diagnosis of lymphoma of B lymphocytes - Malt (BALT). The patient started treatment with chlorambucil and rituximab (Gisl protocol) and today he is in RC with PET negative.

Discussion: BALT originates from the marginal zone and by invading the bronchial epithelial tissue, gives rise to the lymph epithelial lesion. A majority of the patients are asymptomatic and pulmonary lesions are incidental discovery. The disease is often localized, responds favourably to local treatment, has a favourable prognosis and is associated with long-term survival.

Conclusion: The two diseases of lymphoma were simultaneous at the time of diagnosis and conventional treatment for the Hodgkin's lymphoma hadn't led to remission of BALT. Probably the treatment with Rituximab, given for CD 20+, associated with chlorambucil, has contributed to the remission of BALT. We report this case for its peculiarities and its extreme rarity.

482 ORBITAL NON HODGKIN LYMPHOMA (NHL)- CHARACTERISTICS AND EVOLUTION OF 46 CASES FROM TWO ONCOLOGIC CENTRES IN BUENOS AIRES ARGENTINA

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Introduction: Orbital location of extranodal NHL are uncommon, represents 2 a 5% of extranodal LNH and 8-11% of orbital tumors. Published reports usually comprise a reduced number of patients.

Material and Methods: Out of a total of 463 extranodal NHL registered at M. Curie Hospital and H. Moore Institute in Bs. As., 1991 to 2007, orbital location account for 46 patients (9.93%). This unusual value is due to selective referal of oncologic ofthalmologic pathologies. Staging include CT scan of thorax, abdomen and pelvis, orbital CT scan or MRI, bone marrow biopsy. Diagnosis was made by citology or surgical biopsy specimens and immunohistochemistry technics.

Results: Range of age: 17 to 93 years, average 59.78. Male/ female: 1/0.8. Location: conjunctiva 28 (60.86%), eyelid 13 (28.26%), lachrymal gland 5 (10.86%). In left orbit: 50.0%, right: 41.3%, bilateral 8.7%. Inicial symptoms: orbital mass 18 (39.13%), proptosis 12 (26.08%), ptosis 6 (13.04%), eyelid edema 3 (6.52%), epiphora 2 (4.34%), diplopia 1 (2.17%). Subtypes: MALT 20 (41.30%), lymphocytic 8 (17.39%), DLBC 5 (10.87%), follicular 4 (8.70%), lymphoplasmacytic 2 (4.34%), unclassified 8 (17.39%). Time from initial symptoms to diagnosis above 12 months in 67% (range 3-60). Treatment (41 patients): CT (CVP/CHOP) 34 (82.92%), plus radiotherapy in 26 and alone in 6, one case Rituxan. Complete remission (CR) was reached in 88% and PR in 12%. Relapses: local in 4 cases and systemic in 6, with progression and death in 4 cases. Survival was: 1-24 months: 10 cases, 25-60: 12 cases, 60-121: 9 cases. 15 patients without follow up.

Conclusions: We emphasize the delay until diagnosis probably caused by non characteristics initial symptoms and the scarce frequency in this type of NHL. Presentation in 5° to 7° decade, low grade subtypes, initial symptoms: painless mass and proptosis and prevalent location in conjunctiva and eyelid, are comparable with other records. The high rate of complete remissions with chemo and radiotherapy and extended survivals, are characteristics of a good prognosis location of extranodal NHL.

483 RAISED LEVELS OF CXCL12 AND CXCL13 IN CEREBROSPINAL FLUID OF PATIENTS WITH CNS LYMPHOMA

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Background: Homing of malignant lymphocytes to the CNS may play a role in the pathogenesis of CNS lymphoma (CNSL). Chemokine receptors CXCR4 and CXCR5 are expressed in CNS lymphoma. We examined the levels of corresponding chemokines CXCL12 and CXCL13 in the cerebrospinal fluid (CSF) of CNSL patients.

Methods: Matching CSF and serum samples from 23 patients with CNS lymphoma and control samples from ten patients with brain tumors, hydrocephalus or other conditions were collected. Chemokine concentrations were measured using commercially available ELISA kits (Quantikine Immunoassay, R&D Systems, Minneapolis) according to the manufacturer's instructions. Results were confirmed by duplicate measurements.

Results: Median CSF concentrations of CXCL12 and CXCL13 were significantly higher in patients with CNS lymphoma compared to controls (Table). Median serum CXCL12 levels were higher in CNSL patients (2117 vs. 1316 pg/ml, p=0.03) whereas CXCL13 levels did not differ in patients and controls (70 vs. 59 pg/ml, p=0.02). There was no correlation of serum and CSF levels for both chemokines. In three CNSL patients serial CSF samples could be analysed during successful chemotherapy, observing a 1.3 to 10-fold decrease of chemokine concentrations.

Conclusion: CXCL12 and CXCL13 can be measured in the CSF of CNS lymphoma patients at higher concentrations. The increase of CSF CXCL13 in CNSL patients considering the low serum levels points to a production within the CNS, possibly by the tumor or the environment. Further analyses are needed in order to define the role of both chemokines in CNSL and to establish their value for diagnosis and follow up.

	CSF levels in pg/ml: median (range)		
	controls	CNSL	p
CXCL12	115 (0-2442)	528 (83-2080)	0.016
CXCL13	17 (1-187)	527 (18-1465)	0.000027

484 ISOLATED BRAIN RELAPSE OF SYSTEMIC NON-HODGKIN LYMPHOMA: TUMOR RESPONSE AND SURVIVAL IN PATIENTS TREATED WITH ENHANCED CHEMOTHERAPY DELIVERY TO THE CNS

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Introduction: Isolated brain parenchyma relapse, a rare complication of systemic non-Hodgkin lymphoma, is potentially treatable. Long-term survival is possible in some patients.

Methods: We retrospectively reviewed patients with isolated brain relapse treated with enhanced chemotherapy delivery to the CNS (blood-brain barrier disruption [BBBD]) at OHSU, between 1980 and 2007. Eligible patients had CR following initial treatment of systemic lymphoma; none had brain, spine, or leptomeningeal involvement at systemic diagnosis. Information regarding patient characteristics, management and outcomes was collected.

Results: 8 patients (6M/2F) were identified. Median age was 54 yrs (34-65 yrs). 4/8 had ECOG PS greater than 2. Diagnostic brain tumor specimen was obtained in 7/8 patients; tumor histology was large B-cell lymphoma in 7/8. Treatment for brain relapse was BBBD with methotrexate-based chemotherapy (IA) (2.5 gm/day for 2 consecutive days every 4 wks, for up to 12 mon). 6/8 patients achieved CR in the CNS. 2/6 who achieved CR underwent consolidation with HDCT with peripheral blood stem cell (PBSC) or bone marrow transplantation. 4 patients treated with BBBD alone who achieved CR survived 1.3, 1.5, 2.2+, 3.5 yrs after relapse. One patient who received HDCT with PBSC transplantation is alive 8.0 yrs after relapse, and 1 died of septic shock. 2/8 achieved PR after BBBD and survived 0.9, 4.2+ yrs. 4/8 died of disease progression, either CNS (3/8) or CNS/systemic (1/8). The most prevalent BBBD complications were hematologic; non-hematologic included sepsis, respiratory infection, steroid-induced confusion, and cerebellar stroke (one patient each).

Conclusions: In this small series retrospective review, CNS directed therapy yielded encouraging tumor response and survival, warranting further investigation. Similarly, in patients with isolated brain relapse who achieve CR after BBBD, with no evidence of systemic disease, the need for consolidation with HDCT with transplantation remains a question that warrants further study.

485 PROGNOSTIC FACTORS IN THE RELAPSED OR PROGRESSED PRIMARY CNS LYMPHOMA PATIENTS RECEIVED UPFRONT HIGH DOSE METHOTREXATE BASED CHEMOTHERAPY

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Introduction: We evaluated the predictive marker for OS in the relapsed or progressed PCNSL patients initially treated with HD-MTX based CTx with or without RTx.

Material and methods: 188 PCNSL patients (median age 50 years) received HD-MTX (>1 g/m^2) based CTx were collected at 17 institutions in Korea. Among them, 35 patients (19%) were relapsed and 29 patients (15%) were progressed after a median follow-up of 19 months from initial HD-MTX based CTx. The median PFS was 17.8 months in the patients with relapse and 5.1 months in the patients with progression.

Results: The median age at relapse or progression was 49 years. 55 patients (86%) had isolated CNS, 7 isolated systemic, and 2 both CNS and systemic relapse or progression. There were 23 (36%) patients with ECOG ≥2 and 26 (41%) patients with involvement of deep structures at relapse or progression. 52 patients (81%) received treatment: 30 (47%) systemic CTx alone, 10 (16%) RTx alone, and 10 CTx + RTx. The median OS after first relapse or first progression was 20.5 months. Treatment for relapse (versus no treatment, P=0.01) was an independent prognostic factor for OS after relapse or progression in multivariate analysis. Among the 35 relapsed PCNSL patients, longer PFS (≥12 months) and CR to salvage treatment were significant prognostic factors predicting improved OS after relapse in multivariate analysis (P=0.02, 0.01).

Conclusions: Salvage treatment for relapsed or progressed PCNSL patients should be performed for improving OS and longer initial PFS (≥12 months) or CR to salvage treatment might be good prognostic markers for OS after relapse or progression. Other prognostic markers for initial PCNSL patients including age, ECOG, LDH, CSF protein, and involvement of deep structures were not important factors in the relapsed or progressed PCNSL patients.

486 ACUTE ONSET OF SEVERE BRAIN EDEMA DUE TO INTRAVENOUS TREATMENT OF RITUXIMAB (RX) IN A PATIENT WITH PRIMARY CENTRAL NERVOUS SYSTEM (PCNS) LYMPHOMA - CASE REPORT

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Introduction: After intravenous administration (Ad), the cerebrospinal fluid (CSF) levels of Rx have been reported approximately 0.1% of serum levels. The safety, effectiveness and pharmacokinetics of direct intrathecal Ad of Rx in monkeys and also in patients with recurrent lymphomatous meningitis have been investigated in various studies. But we recently experienced a PCNS lymphoma case which represented acute severe brain edema immediately after intravenous treatment of Rx.

Patient: A 56-year-old man presented left progressive hemiplagia. CT scan and magnetic resonance imaging revealed a tumor of 2cm in diameter at the deep portion of white matter in his right cerebral hemisphere. Clinical course: CD20 positive diffuse large B-cell lymphoma was pathologically diagnosed by CT guided probe biopsy. PET-CT scan showed the clinical stage IA. Combined modality plus Rx was chosen for his treatment strategy. Two weeks after biopsy intravenous Ad of Rx was started according to standard dose and method. Two hours after start of Rx he had increasing headache but interruption of Rx and Ad of osmotic diuretic cleared up his symptom. Resumption of Rx gave rise to headache again with hypertension and after finish of Rx his consciousness declined to coma. Emergent CT scan showed progression of local edema around tumor at basal nucleus and corona radiata, and also severe midline shift. Intensive Ad of steroid and osmotic diuretic were not effective. Emergent surgical open decompression procedure rapidly improved his deterioration. Two weeks after Rx minor shrinking of tumor were recognized. The second and latter cycles of chemotherapy with Rx have been conducted safely and effectively.

Conclusion: This case might be quite rare and no other similar reports could be found in past literature. However this case should remind us risk of causing local edema and increase of intracranial pressure by intravenous Ad of Rx to CNS lymphoma especially in early phase of first Ad. Although Rx might be hard to transit to CSF in general, this case implies that it could increase its permeability to vessels in pathogenic lesion.

487 LIPOSOMAL CYTARABINE IN THE TREATMENT OF PRIMARY OR RELAPSED MALIGNANT LYMPHOMA WITH CENTRAL NERVOUS SYSTEM (CNS) INVOLVEMENT

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CNS involvement of malignant lymphoproliferative disease is a severe condition frequently leading to death. Liposomal cytarabine (LIC) a slow release formula of cytarabine is a new drug for intrathecal treatment of lymphomatous meningitis. The purpose of this study was to retrospectively evaluate the efficacy and feasibility of the drug in a series of fourteen consecutive patients treated with LIC at our institution. The cohort consisted of patients with either primary or secondary central nervous system lymphoma (PCNSL, SCNSL). Median follow-up from first LIC treatment was 8.4 months. The 5 patients diagnosed with lymphomatous meningitis at the time of 1st LIC treatment showed a complete cytological response with no relapse of lymphomatous meningitis. The efficacy in parenchymal disease seemed inferior to the effect observed in leptomeningeal disease. The overall response rate (ORR) for the entire cohort was 58%. A total of 8 patients achieved CR/CRu, of who 1 experienced a parenchymal CNS relapse 15 months after the last LIC treatment. The median follow-up of the 7 patients, who were in continuous CR/CRu, was 13 months (range 5-32 months). Treatment was generally well-tolerated with arachnoiditis and headache being the most common adverse effects related to LIC treatment.

In conclusion, LIC is effective in lymphomatous meningitis, but further studies are needed to show if this has a impact on relapse and survival for patients with PCNSL or SCNSL.

488 CHEMOKINE EXPRESSION PATTERNS IN PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

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Chemokines are small proteins known to function as regulatory molecules in leukocyte maturation, traffic and homing, and development of lymphoid tissues. Numerous chemokines have been identified as attractants of different type of blood leukocytes to sites of infection and inflammation. A vast, ever-increasing literature documents the expression of multiple chemokines in tumours and of chemokine receptors by tumour cells. Nevertheless, it is still matter of debate the function of chemokines in tumour develop and growth. We have hypothesized that homeostatic and inflammatory chemokines, which control cell trafficking in secondary lymphoid organs (CXCL13, CXCL12, CCL21), might play a crucial role in the development, progression, and impaired immune response observed in extranodal lymphomas, and in particular in primary CNS lymphoma (PCNSL). Immunohistochemical analysis and *in situ* hybridization on 25 cases of PCNSL revealed a high protein expression of CXCL12, which can also function as survival factor for malignant B cells. In addition, we have characterized the cells of the immune system within the tumour microenvironment and assess the expression of selected inflammatory chemokines. The *in vitro* analysis of chemokine responses induced in a cell line derived from a diffuse large B cell lymphoma of activated phenotype (OCI-Ly10) shows that the interplay of inflammatory and homeostatic chemokines present in the tumour microenvironment might strongly influence the migratory capacity of malignant B cells. Chemokine expression patterns of malignant lymphocytes, vascular endothelium, and infiltrating lymphocytes might influence tumour development, localisation, as well as the inflammatory response in the microenvironment.

489 TREATMENT OF PRIMARY CNS LYMPHOMA WITH THE IDARAM CHEMOTHERAPY REGIMEN

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Introduction: Treatment for PCNSL has evolved from whole brain radiotherapy (WBRT) to approaches using combination chemotherapy +/- WBRT. There is no standard schedule but steroids, methotrexate and cytarabine are the most established drugs. The outlook has improved but remains generally poor and the optimum chemotherapy / radiation strategy has yet to be established. The IDARAM chemotherapy regimen was introduced in 1998 by the UK Central and Southern Lymphoma Group, which published encouraging results in 24 patients with primary and secondary CNS lymphomas in 2004. It continues to be used in the UK but further data is not available. This abstract describes the outcome of 36 HIV -ve patients with PCNSL treated with IDARAM.

Patients and methods: 36 patients with PCNSL diagnosed from 1999 to 2007, whose initial therapy was with IDARAM were analysed. Median age was 57 (range 36-77, with 22/36 aged less that 60yrs). IDARAM (28 day cycle) consists of: idarubicin 10 mg/m^2 IV days1+2; dexamethasone 100 mg IV days 1,2+3; cytarabine 1.0 g/m^{2}IV days 1+2; methotrexate 2.0 g/m^2 (over 6hrs) day 3 and intrathecal cytarabine and methotrexate on days 1 and 8. 2-4 cycles were intended depending on response and tolerance, followed by WBRT.

Results: Follow up is 3 months to 8 years. All patients had marked haematological toxicity (mainly grade 4), requiring planned in-patient care. Response data is available for 26 patients and showed: CR(10), PR(11), SD(1), PD(4) to IDARAM + WBRT. Best response was seen after IDARAM alone in most cases. 14 of the 36 patients are alive (39%). 7 died early in therapy, 3 from toxicity and 4 from disease, receiving only 1 course of IDARAM. Most (24) had 2 courses, 4 had 4 courses and 1 had 3. All but 2 (excluding the 7 early deaths) had WBRT. 18 of the 36 patients were diagnosed 2 years or more ago, allowing some insight into durable survival. Of these, exactly one third are alive in continuing remission.

Conclusions: IDARAM + WBRT is in common use in the UK but data is limited. The regimen is suited to younger / fitter patients with curative intent. Excellent initial responses are seen, as is durable survival for a significant minority. Updated survival data, toxicity and neurocognitive information will be presented.

490 RADIOTHERAPY FOR OCULAR ADNEXAL NON-HODGKIN LYMPHOMA: REPORT OF 32 CASES

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Introduction/background: Primary ocular adnexal lymphoma is rare disease. We evaluated the effectiveness and the toxicity of radiation treatment in patients with primary ocular adnexal lymphoma.

Materials and methods: Thirty two patients (16 men and 16 women) with ocular adnexal non-Hodgkin lymphoma (NHL) were treated in our department between February 1999 and December 2007. The median follow-up period was 24 months (1-121). Men were 15, women 17. Median age was 61 year (range 28-79). Twenty one patients (65.6%) was primary and eleven (34,4%) was secondary. The lymphoma established by incisional surgical biopsy has been in 21 primary patients from orbit or conjunctiva and in 11 patients with progression diseases by biopsy from peripheral lymph nodes before. 10 patients had stage IE, 22 patients had advanced NHLs in stages II-IV with orbital or conjunctival involvement. 11 patients had a B-cell lymphoma from the MALT system with low malignancy, six patients - mantle cell and six - follicular cell lymphoma, 4 patients with diffuse B-cell NHL, 4 patients had unclassificated lymphoma and one Burkett lymphoma. All patients received radiotherapy 1,2 Gy twice a day, total dose was 30-36 Gy (40 Gy for patients with

"bulk"), 2D planning – 29 patients, 3D planning – 3 patients. Patients stages IE were treated with radiotherapy alone, patients with advanced lymphoma had received chemotherapy too.

Results: All patients had local complete responses (100%). The 2-year local control rate for all patients was 100%. Seventeen patients (53.1%) had acute, radiotherapy-related complications. Acute complications grade 1/2 were documented in 53.1%, acute complications grade 3/4 were not observed. Late effects were in 15.6%. Five patients, treated with doses of >36 Gy, developed grade 3 complications (four (12.5%) cataract, one (3.1%) dryness). Corneal ulcerations, retinal injury were not observed.

Conclusion: Radiotherapy alone proved effective in treating local ocular adnexal lymphoma stage IE. Doses of >36 Gy resulted in an increase of late complications. Radiotherapy is also well tolerated and effective in advanced NHL stages with ocular adnexa involvement.

491 JAPANESE PATIENTS WITH OCULAR ADNEXAL MALT LYMPHOMA

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MALT lymphoma is a distinct type of B-cell lymphoma that develops in extranodal sites and usually has an indolent clinical course as a localized disease. Recent clinicopathological studies suggest a strong relationship between MALT lymphoma and inflammatory diseases of the epithelium such as autoimmune diseases and infections, because chronic antigen stimulation has been causally linked to the development of lymphoproliferative diseases in B cells. MALT lymphoma grows in extranodal lymphoid tissue and exists in epithelium tissues, and it is often difficult to distinguish malignant lymphoid tissue from benign inflammation. However, this is only one of the possible causes; recent positive and negative correlations between ocular adnexal MALT lymphomas and chlamydial infections reported by different researchers indicate several different possible explanations. Here, we analyze twenty-three cases of ocular adnexal MALT lymphoma whose monoclonality was confirmed by immunoglobulin heavy chain gene rearrangement and/or the analysis of cell surface antigens with a flow cytemeter for evidence of expected causative factors, using both ELISA analysis to detect antibodies and Southern blot analysis followed by specific PCR gene amplification. Our series of patients did not show any serological relations to the EB virus, the Hepatitis C virus, or to Chlamydophila psittaci. Two cases had positive serum antibodies for autoimmunity, another two cases had positive antibodies against Chlamydia trachomatis. None of our cases showed the presence of chlamydial 16S rRNA or 16S-23S spacer rRNA genes (C. psittac, C trachomatis, C. pneumoniae, and C. felis) after PCR amplification. These results indicate that the inflammatory agents are still unknown in our series of ocular adnexal MALT lymphomas, and that some types of chlamydial infections are not associated with ocular adnexal MALT lymphoma in southern regions of Japan. The true situation regarding the relation between ocular adnexal MALT lymphomas and chlamydial infections will be clarified by the results of increasing numbers of clinical studies in other countries.

492 RITUXIMAB IMMUNOTHERAPY IN UNTREATED LOW-GRADE INTRA-ORBITAL OCULAR ADNEXAL LYMPHOMA (OAL): A PROSPECTIVE MULTICENTRE PHASE II STUDY

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Introduction: As radiotherapy is the standard treatment for low-grade ocular adnexal lymphomas (OAL), it is associated with toxicities such as cataract, xerophthalmia, and rare retinal complications. We therefore investigated in a prospective multicentre phase II study the efficacy of the anti-CD20 antibody rituximab in untreated intra-orbital low-grade OAL without visual impairment and high tumor burden.

Patients and methods: Since May 2006, 12 patients (pts) have been included in the study.

Results: Pts characteristics were: MALT-type lymphoma in 11 pts and follicular lymphoma in 1 case; median age 57 years; orbital localizations included palpebral and lacrimal gland involvement in 5 (42%) and 3 pts (25%), respectively; bilateral OAL in 1 pt (8%); nodal involvement in 2 pts (17%); stage IV in 5 pts. All pts received four weekly rituximab administrations (375 mg/m^2). No significant side effects have been observed. The overall response rate (ORR) 1 month after treatment completion was 58% with 4 complete remissions (CR) (33%) and 3 partial remissions (25%). Radiotherapy (RT) was performed in all but one (personal refusal) non-responding pts. RT consisted of ophthalmologic tumor irradiation with a median dose of 27 Gy in 16 fractions of 1.8 Gy. The main acute side effects of radiotherapy were palpebral and conjunctival erythema. All 4 pts were in CR after RT. With a median follow-up of 10 months, no relapse or death have been observed.

Conclusions: Rituximab induced an ORR of 58% in untreated intra-orbital low-grade OAL without ocular impact and high tumor burden. A longer patient's follow-up is however warranted to confirm if radiotherapy could be safely and efficiently replaced by immunotherapy.

493 HIGH-GRADE OCULAR ADNEXAL LYMPHOMA: CLINICO-PATHOLOGIC CHARACTERISTICS AND PROGNOSTIC FACTORS OF A SINGLE CENTRE SERIES OF 17 PATIENTS

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Introduction: Ocular adnexal lymphomas (OAL) mainly correspond to a B-cell type and, in 80% of cases of low-grade lymphomas. Only 15% of them are considered of high-grade.

Patients and methods: We retrospectively investigated the clinico-pathologic features and outcome of a series of 17 high-grade OAL patients (pts) treated at the Institut Curie.

Results: Pts characteristics were: Histopathological review (WHO classification) found 14 diffuse large B-cell lymphoma (78%), 1 Burkitt-like lymphoma, and 2 Burkitt's lymphomas; Male/Female sex ratio 1.4; median age 63 years (range: 49-86); PS >1 18%; ophthalmologic localizations were intra-orbital in 9 pts (53%), lacrimal gland in 4 pts (23%), conjunctival and palpebral in 2 pts (12%), and bilateral OAL in 3 pts (18%); nodal involvement 29%; stage IV 59% with 4, 3, 2, 2, 2 and 1 bone marrow, central nervous system, gastric, waldeyer's ring, lung, and splenic involvements, respectively; more than 2 extranodal sites 35%; elevated serum LDH level 25%; the International Prognostic Index was 0-1, 2, and 3 in 35%, 29%, and 35% of cases, respectively. All but one pts received a first line of chemotherapy with rituximab in 5 cases. Ophthalmologic radiotherapy was performed in 8 pts. At the end of the first treatment line, 12/15 evaluable pts were in complete remission (CR), 2 in partial remission, and 1 had a stable disease. With a median follow-up of 144 months (range: 7-171), 8/14 evaluable patients were alive in continuous CR and 6 were dead in whom 5 of lymphomatous progression. The 5-year overall survival (OS) was 53%. In univariate analysis, the only one factor correlated with a lower OS was a PS >1 ($p = 0.004$).

Conclusions: Despite a high proportion of disseminated localizations, high-grade OAL seems to have a similar OS than nodal high-grade B-cell lymphomas.

494 NON-GASTRIC MALT LYMPHOMAS A SINGLE CENTER EXPERIENCE ON 75 PATIENTS

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Introduction: Extranodal marginal zone B-cell lymphoma (EMZL) of mucosa associated lymphoid tissue (MALT) is an indolent disease. Non- gastric MALT lymphomas may arise in any anatomic site.

Patients and Methods: 75 consecutive patients (pts) with the diagnosis of non-gastric EMZL according to the WHO classification criteria, confirmed after histological reevaluation were analysed. Disease localization was correlated with clinical and laboratory features, treatment modalities and outcome.

Results: Pts' median age was 55 years. The most commonly affected sites were salivary glands (19), skin (14), ocular adnexa (13), lung (10), intestine (8) and Waldeyer ring (6). Ann Arbor stage I disease was present in 39 pts (52%), stage II in 9 (12%) and stage IV in 27 (36%). 16 pts (21%) had involvement of more than one extranodal site. Lymph node and bone marrow involvement were present in 16% and 11% respectively. Most pts (90%) were in the low or low-intermediate risk groups according to the International Prognostic Index (IPI). B-symptoms were present in 6 pts (8%). Pts were treated with several modalities, including chlorambucil alone or in combination with other agents including Rituximabin 44 pts. Complete and partial remission was achieved in 77% and 7% respectively, with an overall response rate of 84%. After a median follow up of 51 mos (range 2-228) the 5- and 10-year overall survival (OS) were 93% and 88% respectively. Lung localization was associated with inferior outcome, with a 5- and 10-year OS of 83% and 56% respectively.

Conclusions: Non-gastric MALT lymphomas are a disseminated disease in at least one third of the pts. The optimal management may be site-related. Chlorambucil in combination with Rituximab seems to be an effective treatment strategy. Pts with lung involvement have a less favorable outcome.

495 COMBINED IMMUNO-CHEMOTHERAPY WITH RITUXIMAB, METHOTREXATE, CCNU, AND PROCARBAZINE FOR THE TREATMENT OF PRIMARY CNS-LYMPHOMA IN THE ELDERLY

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Introduction: Primary CNS lymphoma (PCNSL) have a dismal prognosis despite initial response to steroids and whole brain radiotherapy (WBRT). Addition of high-dose methotrexate (MTX) to WBRT has improved the prognosis of patients (pts.) with PCNSL, resulting in median survival rates of up to 60 months (mo). Surviving pts, particularly elderly treated with combined radio-chemotherapy are at substantial risk of developing leukoencephalopathy. There have been ambiguous observations on response of PCNSL to the anti-CD20 monoclonal antibody rituximab in small treatment series. Here we report the results of 16 pts treated with rituximab, MTX, CCNU and procarbacine (R-MCP protocol) within a monocentric pilot-study.

Patients and Methods: Pts. >65 yrs received up to 3 cycles of the R-MCP protocol: rituximab (375mg/m^2, d -6, 1, 15, 29); MTX (3g/m^2, d2, 16, 30); procarbazine (60 mg/m^2 p.o., d1-10) and CCNU (110 mg/m p.o., d 1); cycles were repeated every 42 days. There was no lower limit of Karnofsky Performance Status (KPS). Inclusion criteria were age >65 yrs and biopsy proven PCNSL.

Results: Sixteen pts. (median age 76 yrs., range 65-83 yrs.) were treated with the R-MCP protocol in this pilot-phase. In 5 pts MTX was not tolerated after 1 (n=4) and 2 (n=1) applications due to hepatic (n=1) and renal impairment (n=4). In these pts, treatment was continued with rituximab, CCNU and procarbacine. Objective response was seen in 15 of 16 pts. (93,7%) with 11 CR and 4 PR. One pt died due to pulmonary embolism 2 weeks after initiation of treatment and was not evaluable for response. Two pts with refractory disease could successfully be salvaged. Two further pts experienced fatal relapse. After a median follow-up of 11 mo (range, 1-19) 13 of 16 pts (81.25%) are alive and disease-free. Preliminary evaluation shows a 12-mo overall survival of 86.7%. Severe leukoencephalopathy as well as grade IV toxicity could not be observed.

Conclusion: The immuno-chemotherapy protocol presented here is safe and shows high efficacy in treating elderly pts. with PCNSL. The addition of rituximab to MTX-based chemotherapy is promising and warrants further investigation. A prospective phase-II trial will be initiated.

496 PRIMARY BREAST NON-HODGKIN'S LYMPHOMA: A LARGE SINGLE CENTER STUDY OF INITIAL CHARACTERISTICS, NATURAL HISTORY, AND PROGNOSTIC FACTORS

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Introduction: Primary breast lymphoma (PBL) is a rare site of this disease. This peculiar extra-nodal site raises three main questions, namely (1) their clinical and biological features, (2) the prognostic impact of breast involvement on the natural history of the disease, and (3) the risk of central nervous system (CNS) relapses. Therefore, the aims of this study were to define the initial pathological and clinical characteristics, and prognostic factors of patients with primary breast malignant lymphoma (PBL).

Patients and methods: All patients treated at the Institut Curie for lymphoma with breast involvement were retrospectively reviewed. A pathological review of all cases was performed, including Bcl-2 and CD10 expressions.

Results: Forty-six cases were selected for the study in whom 40 cases of high-grade NHL. A complete analysis was then performed on these 40 high-grade NHL patients. 21/29 cases (72%) of cases were Bcl-2 positive and 5/29 (17%) of cases were CD10 positive. Peculiar initial characteristics showed nodal involvement in 57% cases and 2 or more extra-nodal sites in 32% of cases. At the end of initial therapy, 36 patients (90%) achieved CR. With a median follow-up of 96 months, nineteen patients (47%) relapsed in whom 3 in CNS site. The 5-year disease-free (DFS) and overall survivals (OS) were 54 % and 61%, respectively. In multivariate analysis, the presence of 2 or more extranodal sites was prognostic for lower DFS (p=0.0008) and OS (p=0.09), and a PS ≥1 was prognostic for lower OS (p=0.005). Finally, when our series was compared to a historical series of 111 patients with aggressive nodal lymphomas, we observed significant lower survival rates in localized PBL (p<0.03).

Conclusions: Initial breast localization has a pejorative impact on the outcome of NHL patients, with an impressive adverse influence of additional extranodal sites. These results therefore suggest a specific management of PBL.

497 BREAST NON-HODGKIN'S LYMPHOMA: A SINGLE CENTER EXPERIENCE OF 18 PATIENTS

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Introduction: Breast non-Hodgkin's lymphoma accounts for 0.5-1% of all cases of extranodal lymphoma. Although generally localized, a significant relapse rate is observed. There is no consensus about therapy and most patients receive chemotherapy with good response.

Material and Methods: We retrospectively analyzed a series of patients with breast lymphoma seen at our institution over a 7-year period, between 2000 and 2006. The aim of the study is to determine clinical characteristics of such patients, and to evaluate impact of treatment on survival.

Results: There were 18 patients, with a median age at 64 years. All patients present with unilateral disease. Histology showed a diffuse large B-cell lymphoma type predominance. Localized disease was noted in 13 cases (stage IE) and 5 patients were at stage IIE. All patients received chemotherapy with (11) or without rituximab (7). Chemotherapy was mainly CHOP. A complete response (CR) was achieved in 17 patients. A relapse was observed in 27% of patients, in particular in central nervous system.

Conclusions: Breast lymphoma may be considered as a distinct entity. It was mainly high grade lymphoma and represents the only manifestation of the disease. Prognosis remains favourable but progress is still needed. Updated results will be presented at the meeting.

498 BRONCHIAL-ASSOCIATED LYMHOID TISSUE (BALT) LYMPHOMA - THE THERAPEUTIC EFFECT OF MONO CHEMOTHERAPY

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Background: Bronchial associated lymphoid tissue (BALT) lymphoma is a rare subtype of low grade B cell marginal zone non Hodgkin's lymphoma. BALT represents 3.6% of all extranodal lymphomas and 0,4% of all non Hodgkin's lymphoma. The purpose of this study was to analyzed the diagnosis and the treatment of BALT-oma.

Material and methods: This study included six patients who had BALT lymphoma diagnosed between January 2001 and April 2007 at the Institute of hematology CCS, Belgrade. Demographic characteristics were as follow: male/ female ratio was 1:5 (16.67%:83.33%); the median age was 63 years (range, 37-72). On presentation, four patients (66.66%) had nonspecific respiratory symptoms and all of them had B symptoms. Patients were seronegative for human imunodeficiency viruses (HIV and hepatotropic viruses HCV and HBsAg). One patient had Sjogren's syndrome and one pulmonary tuberculosis. The diagnosis was based on open lung at one patient or transbronchial biopsy at 5 pts. Patohistological findings suggested lymphoma of marginal zone and immunohistological profile confirmed the diagnosis: CD20+/ CD10Ø/CD5Ø/Cyclin D1Ø/CD23Ø/IgMØ. According to the Ferraro staging clinical classiffication four patients (66.66%) had localized disease (stage IE-IIE) and two had stage IIIE. Three patients (50%) had ECOG performance status (PS) 0 and three patients had a PS 1. Five patients (83.33%) received chemotherapy consisting of chlorambucil alone (doses was 10 mg p.o. during ten days monthly up to 6 cycles). One patient underwent surgical resection, followed with chlorambucil.

Results: A complete response with initial therapy was achieved in one patient (16.67%) and a partial response was obtained in five patients (83.33%). All the patients were alive during the median follow-up period of 39 months (range 6-72 months). During the follow up period one patient relapsed into other extranodal localization, but achived PR after CHOP regimen.

Conclusion: BALT lymohoma tends to be localized disease at the time of diagnosis, responds well to surgical treatment or mono chemotherapy with chlorambucil and has a favourable prognosis.

499 NHL'S EXTRANODAL INVOLVEMENT IN HCV POSITIVE PATIENTS: CUTANEOUS B-CELL NHLS

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Introduction/Background: extranodal involvement is frequent for patients with HCV-related NHL (65% versus 19% in non-HCV related lymphomas). Target organs seem to be salivary glands and liver, according to the virus-trophism. Moreover, up to 40-74% of HCV positive patients develop an extrahepatic involvement during their infection's history. Of particular interest is the prevalence of marginal zone lymphoma in HCV positive patients, as response to the chronic infection with immunological activation and expansion of marginal zone B-lymphocite.

Material and Methods: all new NHL's affected patients are tested for HCV serology, molecular biology with viral load and genotyping. Staging is according to Ann-Arbor stage.

Results: 11 consecutive HCV-rnapositive patients are detected with cutaneous B-NHL. Patients are 8 female, 3 male, median age at diagnosis is 70 years, viral load result high (over 2.5 milion UI/ml) in 4/7 patient valuables, genotype is: 6 type 2, 2 type 1b, 3 type 4. Follow up NHL'S hystotype according to the REAL classification is: 6 marginal zone lymphoma (4 with nodal involvement, 2 primitive cutaneous), 3 follicular grade 2 lymphoma, 1 diffuse large B-cell and 1 mantle cell lymphoma. The group with indolent behavior have a long survival (until 10 years FU), in contrast to a poor prognosis for group with large-B cell and mantle cell lymphoma.

Conclusions: NHL in HCV infected patient present frequently an extranodal localization at onset. In our experience 11 consecutive HCV-rna positive patients present at onset a cutaneous involvement of B-cell NHL. These represent notable for the not usual organ (skin) and for the B-lineage of lymphomas, instead of usual prevalence of T-cell cutaneous NHL (75% of cutaneous NHL). The proposal is of a particular interest for these patients as subset of HCV-related B-NHL and eventual acquired dermotrphism for B-lymphocyite during chronic immunologic stimulation and lymphomagenesis.

500 AUTOIMMUNE COMPLICATIONS ARE FREQUENT IN SPLENIC AND NODAL MARGINAL ZONE LYMPHOMAS

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Introduction: Splenic (SMZL) and nodal marginal zone lymphomas (NMZL) are rare indolent disorders with a reported incidence of autoimmune complications (AIC) of 10 to 15%. We retrospectively evaluated our series of SMZL and NMZL to assess the frequency and characteristics of AIC, their relationship with clinical and biological parameters and their impact on the disease course.

Patients and Methods: We analyzed 143 patients, 86 males, 57 females, median age 63, diagnosed at our Institutions. SMZL were 117, NMZL 26. Diagnosis was based on histological and immunohistological analysis of spleen (45 cases) and/or bone marrow in SMZL, of lymphnodes in NMZL. Anti-HCV seropositivity (RIBA) was detected in 26/122 (21.3%) tested patients.

Results: Clinically relevant AIC occurred in 34/143 (23.8%) patients: autoimmune haemolytic anaemia (AIHA) in 12, autoimmune thrombocytopenia in 6, Evans' S. in 2, autoimmune pancytopenia in 2, anti-MAG neuropathy in 3, Sjoegren's S. in 3, rheumatoid arthritis in 2, symptomatic crioglobulinemia in 2, Sweet S. and glomerulonephritis in 1 respectively. In 2 cases with AIHA antiphospholipid syndrome coexisted. Of the remaining 109 patients, 88 were laboratory screened for autoimmunity; 26 of them (29.5%) were positive (Rheumatoid Factor or ANA 11, asymptomatic crioglobulinemia 11, LAC 4). The incidence of AIC was significantly higher in females and in patients aged <60 years. No significant correlations were found between AIC and: spleen size, LDH or beta2-microglobulin levels, anti-HCV seropositivity and leukemic phase. In 19/34 patients AIC occurred at presentation, in 7 they preceded the diagnosis of lymphoma of 3 to 94 months. Symptomatic AIC were treated with: steroids ± alkylating agents (16), splenectomy (5), Rituximab ± chemotherapy (4), alkylating agents (2), other drugs (2). Median survival of all patients was 113 months; it was not significantly influenced by the occurrence of AIC.

Conclusions: Clinical and laboratory autoimmune phenomena were frequent in our series of SMZL and NMZL, overall affecting more than 40% of patients and mostly occurring at diagnosis or even before, but apparently not influencing survival.

501 RITUXIMAB MONOTHERAPY IN SPLENIC MARGINAL ZONE LYMPHOMA

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Introduction: Splenic marginal zone lymphoma (SMZL) is an indolent disease with distinct clinical, morphological and immunophenotypic features. Splenomegaly can be marked in this condition and yet lymphadenpathy may be quite inconspicuous. No treatment may be necessary at the outset. If the size of the spleen, the development of pancytopenia or other clinical complications demand an intervention, splenectomy is considered the treatment of choice. The median time to progression has been reported as 32 months after this procedure. Splenectomy however, is not without risk particulary in elderly patients and there is a long term increased susceptibility to infection. As the neoplastic cells in this condition usually strongly express CD 20, we decided to treat patients with this disorder with Rituximab, an anti-CD 20 chimeric monoclonal antibody.

Material: 15 patients who were diagnosed to have SMZL according to accepted criteria were treated with Rituximab.This was used as a single agent at a dose of 375 mg/m^2 for four to eight consecutive weeks.

Results: 14 of the 15 patients responded to this infusion often with a dramatic reduction of a massively enlarged spleen and correction of the pancytopenia. The mean progression free survival of these responding patients is 39 months (range 3 to 88 months). One patient died at 45 months of unrelated disease and four relapsed. 9 remain progression free at a median of 51 months (range 3 to 88 months).

Conclusion: Rituximab is a highly effective monotherapy for SMZL and can obviate the need for splenectomy with attendant complications. Our data are superior to the results of splenectomy.

502 RITUXIMAB MONOTHERAPY FOR SPLENIC LYMPHOMA WITH VILLOUS LYMPHOCYTES

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Introduction: Splenic lymphoma with villous lymphocytes is a indolent lymphoma recognized within the WHO classification as a distinct entity among marginal zone lymphoma. No consensus was established for the treatment of this lymphoma, although splenectomy is considered the first line treatment. As villous lymphocytes express the CD20 antigen, treatment with rituximab was recently reported, as monotherapy or combines with chemotherapy.

Material and Methods: We report another case of rituximab monotherapy treatment for a patient with splenic lymphoma with villous lymphocytes, inducing a complete remission.

Results: A 50-year-old woman was diagnosed with indolent B-cell non-Hodgkin's lymphoma because of presence of B signs with splenomegaly and supra centimetric sus diaphragmatic adenopathies. Staging show a stage II with mediastinal bulky. Definitive histological diagnosis was difficult with characteristics of follicular lymphoma and marginal zone lymphoma. It was decide to treat the patient with 6 monthly courses of CHVP chemotherapy. A complete remission was obtained after the fist 6 courses of chemotherapy. Then, the patient received 6 courses of CHVP every two months for one year. A relapse was noted after 14 months of follow up. The patient presented with symptomatic splenomegaly and circulating abnormal lymphocytes. Computed tomography revealed no profound adenopathy. Cytologic evaluation of lymphocytes concluded to typical villous lymphocytes with concordant phenotype of villous lymphocytes. Treatment was decided because of symptomatic splenomegaly. Since the refused of patient for splenectomy, we decided to manage this patient with rituximab monotherapy. The patient received rituximab at a dose of 375 mg/m^2 once a week for 4 consecutives weeks. Evaluation after the four weeks showed clearance of villous lymphocytes, disappearance of splenomegaly and normalisation of LDH and beta 2 microglobulin. After one year of follow up, the patient is still in complete remission.

Conclusions: Rituximab monotherapy for splenic lymphoma with villous lymphocytes is a safe and efficient treatment. It could replace splenectomy as a good palliative procedure, especially in elderly patients.

503 AUTOIMMUNITY IN LYMPHOPLASMACYTOID LYMPHOMA (LPL) AND MARGINAL ZONE LYMPHOMA (MZL)

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Background: LPL and MZL share clinicopathological features including the frequent production of monoclonal IgM serum proteins. LPL cells are polireactive to microbic and autoantigens, through T-independent and dependent pathways. Also MZL cells often show auto- and cross-reactive repertoire and hyperreactivity to activation. Indeed autoimmune manifestations seem to be frequent inLPL and MZL.

Aim: To evaluate the incidence of autoimmune manifestations and compare their frequency and clinical significance in pts with LPL and MZL.

Methods: Clinical and immunological data were retrieved and compared in the pts with MZL and LPL consecutively diagnosed at our Institute from January 1995 to December 2006.

Results: Among 87 pts, 43 LPL and 44 MZL (29 splenic, 15 nodal), 48 were male (55%, 25 LPL and 23 MZL). The median age was 65 (32-85) (67 in LPL, 61.5 in MZL). HCV-RIBA was positive in 13 pts (3%LPL, 10% MZL P=NS). HBV-DNA was positive in 5 pts (1 LPL, 4 MZL P=NS), while 31 (14 LPL, 17 MZL P=NS) had HBV-positive serology without HBV-DNA positivity. Other viral infections were detected in 9 pts, CMV being the most frequent, with no differences among LPL and MZL. Sixty-two pts had monoclonal IgM proteins (41/43 LPL (95%), 21/44 MZL (48%) P<0.0001). Thirty-seven pts (18 LPL, 19 MZL) had autoimmune manifestations (M/F 19/18 P=0.5), 16 of them (8 LPL, 8 MZL) of clinical significance (M/F 5/11 p<0.05). In particular 6 pts had autoimmune haemolytic anemia (1 had also Hashimoto disease and connectivitis), 2 anti-MAG positive peripheral neuropathy, 2 Raynaud disease, 2 Sjogren syndrome; 1 each autoimmune thrombocytopenia, scleroderma, Sweet syndrome and rheumatoid arthritis. The most frequent subclinical autoimmune manifestations were hypocomplementemia (35%), Coombs-positive test (27%) and

cryoglobulinaemia (14%). Autoimmunity did not correlate with viral infections nor with the production of monoclonal IgM serum proteins. Median overall survival (MOS) of all pts was 112 months (LPL 125 and MZL 112 months, respectively; P=NS) and did not differ in pts with autoimmunity.

Conclusions: Autoimmunity is frequent both in LPL and MZL, particularly in females. However it does not seem to be related to the more frequent production of IgM proteins in LPL, nor to common viral infections and does not impact on survival.