419 CLINICAL FEATURES OF EXTRANODAL MARGINAL ZONE LYMPHOMA OF MUCOSA-ASSOCIATED LYMPHOID TISSUE

Y. Yamamoto[1], N. Tomita[1], H. Takasaki[2], E. Ogusa[3], Y. Hattori[4], S. Matsuura[5], C. Matsumoto[6], S. Takemura[7], H. Kuwabara[8], Y. Ishigatsubo[1]
[1]Department of Internal Medicine and Clinical Immunology, Yokohama City University Graduate School of Medicine, Yokohama, Japan, [2]Department of Oncology, Kanagawa Cancer Center, Yokohama, Japan, [3]Department of Hematology, Yokohama City University Medical Center, Yokohama, Japan, [4]Department of Hematology/Immunology, Fujisawa City Hospital, Fujisawa, Japan, [5]Department of Hematology, Shizuoka Red Cross Hospital, Shizuoka, Japan, [6]Department of Hematology, Yokosuka City Hospital, Yokosuka, Japan, [7]Department of Internal Medicine, Yokohama Ekisaikai Hospital, Yokohama, Japan, [8]Department of Hematology, Yamato Municipal Hospital, Yamato, Japan

Background: The clinical manifestations of extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) remain unclear. We studied patients with MALT lymphoma by our group.

Patients and Methods: The Yokohama City University hematology group newly diagnosed 133 patients with MALT lymphoma between 1998 and 2010. We retrospectively studied 124 for whom complete clinical data were available at presentation, and who had undergone tumor staging at least by physical examination; computed tomography (CT) from cervix to pelvis (or positron emission tomography/CT); bone marrow aspiration; and biopsy.

Results: Slight female predominance (men, 58; women, 66) was observed in the study population; the median age was 67 years (range: 37-81 years). The primary dominant locations at presentation were the stomach (39%), orbita (20%), lung (13%), intestinal tract (8%), thyroid gland (6%), others (12%), and unknown (2%). Most patients had localized disease (stage 1, 65%; stage 2, 19%; stage 3, 6%; stage 4, 10%). The soluble interleukin -2 receptor level was over 1,000 U/ml in 10 patients (8%), and the serum lactate dehydrogenase level was elevated in 20 patients (16%). Of the 124 patients, 14 (11%) had lymph node involvement; 5 (4%), bone marrow involvement; and lung and gastric involvement. Four of 8 patients with primary thyroid MALT lymphoma had regional lymph node involvement. According to the International Prognostic Index criteria, 66%, 24%, 9%, and 1% of the patients were in the low-, low-intermediate, high-intermediate, and high risk groups, respectively. Chromosomal analysis was performed for 28 patients; 5 (18%) had cytogenetic abnormalities, including t(11;18) in 1 patient. The 5-year overall survival rate for all 124 patients was 96.1%.

Conclusion: MALT lymphoma had slight female predominance, and most patients had localized disease stage. The vital prognosis was excellent. Gastro-intestinal fiberscopic examination is essential especially in cases with lung involvement at presentation.

420 CLINICAL MANIFESTATIONS OF PRIMARY PULMONARY EXTRANODAL MARGINAL ZONE LYMPHOMA OF MUCOSA-ASSOCIATED LYMPHOID TISSUE

E. Ogusa[1], N. Tomita[2], Y. Yamamoto[2], H. Takasaki[3], Y. Hattori[4], C. Matsumoto[5], Y. Ishigatsubo[2]

[1]Department of Hematology, Yokohama City University Medical Center, Yokohama, Jordan, [2]Department of Internal Medicine and Clinical Immunology, Yokohama City University Graduate School of Medicine, Yokohama, Japan, [3]Department of Oncology, Kanagawa Cancer Center, Yokohama, Japan, [4]Department of Hematology/Immunology, Fujisawa City Hospital, Fujisawa, Japan, [5]Department of Hematology, Yokosuka City Hospital, Yokosuka, Japan

Background: We studied the clinical manifestations of pulmonary extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma).

Patients and Methods: We retrospectively analyzed the clinical data for 16 patients (men, 11; women, 5) who had untreated pulmonary MALT lymphoma that had been diagnosed between 1998 and 2010 by the Yokohama City University hematology group in Japan. These patients constituted 13% of the 124 patients with untreated MALT lymphoma (complete clinical data available) and 0.7% of the 2,338 patients with untreated lymphoma that had been diagnosed by our group.

Results: Male predominance was noted in this population; the median age was 58 years (range, 34-78 years). MALT lymphoma was suspected on the basis of examination findings in 14 patients, and clinical manifestations in 2. Pulmonary MALT lymphoma was confirmed by lung biopsy under computed tomography for 1 patient, trans-bronchial lung biopsy for 7, video-assisted thoracic surgery for 5, and surgery for 3. The right lung was involved in 4 patients, left lung in 6, and both lungs in 6. Of 7 patients with extrapulmonary involvement, 4 had gastric involvement, and 3, nodal involvement. Chromosomal analysis was performed for 4 patients; chromosomal abnormalities were detected in 2 patients, and t(11;18) was detected in 1. The International Prognostic Index indicated low risk for 8 patients, low-intermediate risk for 4, and high-intermediate risk for 4. Primary treatment involved surgery alone in 2 patients, surgery followed by rituximab (R)-containing chemotherapy in 2, R-containing chemotherapy in 11, and chemoradiotherapy without R in 1. In the median observation period of 28 months (range, 3-113 months), disease progression was recorded in 3 patients, but all 16 patients were alive at the end of the observation period. One patient was treated with 8 courses of R alone and achieved partial remission; the subsequent tentative surgery showed no evidence of residual lymphoma. He has had 72 months of progression-free survival after diagnosis.

Conclusions: Primary pulmonary MALT lymphoma predominantly affects men and has a good prognosis. R has potential as a therapeutic agent in such cases.

421 THYROID MARGINAL ZONE B-CELL LYMPHOMA OF MALT TYPE: CLINICAL MANIFESTATION AND OUTCOME OF A RARE DISEASE- CONSORTIUM FOR IMPROVING SURVIVAL OF LYMPHOMA (CISL) STUDY

S. Oh[1], W. Kim[2], J. Kim[3], S. Kim[2], S. Lee[1], D. Lee[4], H. Kang[5], M. Song[6], H. Kim[7], J. Kwak[8], B. Park[9], Y. Do[10], S. Jeong[11]
[1]Internal Medicine, Dong-A University Hospital, Busan, Korea, Republic of, [2]Internal Medicine, Samsung Medical Center, Seoul, Korea, Republic of, [3]Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic of, [4]Internal Medicine, Asan Medical Center, Seoul, Korea, Republic of, [5]Internal Medicine, Korea Institute of Radiological and Medical Sciences, Seoul, Korea, Republic of, [6]Internal Medicine, Pusan National University, Busan, Korea, Republic of, [7]Internal Medicine, Hallym Medical Center, Seoul, Korea, Republic of, [8]Internal Medicine, Chonbuk National University Medical School, Jeonju, Korea, Republic of, [9]Internal Medicine, Hanyang University College of Medicine, Seoul, Korea, Republic of, [10]Internal Medicine, Dongsan Medical Center, Daegu, Korea, Republic of, [11]Internal Medicine, Ajou University School of Medicine, Suwon, Korea, Republic of

Background: thyroid marginal zone b-cell lymphoma of the malt type (TY-MZL) is an extremely uncommon form of lymphoma. Due to its rarity, the natural history and optimal treatment modality for this disease has yet to be well established.

Methods: from 1989 to 2010, a total of 27 patients with histologically-confirmed TY-MZL were analyzed retrospectively.

Results: the median age of our subjects was 53 (range: 25-82) years. This study involved 15 females (62.5%) and 9 males (37.5%). 88.9% of the patients (24 of 27) initially presented with localized disease, defined by Ann Arbor stage I/II. BM involvement was detected in less than 7.4%. B symptom was observed in only 1 patient. 91.7% of the patients (25 of 27) were categorized as the low or low-intermediate risk group according to the International Prognostic Index (IPI). 95.8% were in the low risk group according to the Marginal Zone Lymphoma Prognostic Index (MZLPI) hashimoto's thyroiditis was accompanied 65% of patients. All of data available patients had been observed normal value in thyroid function test except 1 hypothyroidism. Thyroglobulin level was elevated in 68.4% of patients. 26 patients had been treated with operation, radiotherapy, or chemotherapy. 25 patients had achieved CR. During the follow-up, only 2 patients had been observed progression and no death.

Conclusion: TY-MZL trends to be an indolent disease. But different from other malt site MZL, TY-MZL was well controlled with several treatment modalities and sustained their response for a long time.

422 OUTCOMES FOLLOWING INVOLVED FIELD RADIOTHERAPY (IFRT) WITH OR WITHOUT RITUXAN IN PATIENTS (PTS) WITH EARLY STAGE LOW-GRADE NON-HODGKIN'S LYMPHOMA (NHL) STAGED WITH CT VERSUS PET

J. Lukens[1], S. Nasta[2], E. Glatstein[1], J. Plastaras[1]
[1]Radiation Oncology, Hospital of the University of Pennsylvania, Philadelphia, United States, [2]Hematology Oncology, Hospital of the University of Pennsylvania, Philadelphia, United States

Background: The use of FDG-PET for staging follicular lymphoma (FL) changes the stage in a significant number of pts. To evaluate whether staging with PET translates into improved disease free survival (DFS) for pts with early stage FL, we performed an analysis of CT and PET staging, for pts with early-stage, low-grade NHL treated with IFRT. A secondary objective was to evaluate whether the addition of Rituxan to IFRT improves DFS in this subset of pts, in light of evidence that upfront Rituxan improves progression-free survival in pts with Stage 2, 3 or 4 FL compared to observation alone.

Patients and Methods: Pts with Stage I or II low-grade NHL treated with initial IFRT at our institution between 1992 and 2009 were identified. An IRB-approved

retrospective analysis was undertaken to evaluate staging by CT versus PET. DFS was defined as time from initiation of IFRT to progression, death or last contact alive.

Results: 44 pts were identified; 17 staged by CT, and 27 by PET. Stage I disease was more frequently defined in pts using CT compared to PET, but this difference did not reach statistical significance (94% vs 70%, respectively, p=0.12). The groups were equally matched by FLIPI risk stratification, with most pts falling in the low-risk group. Median follow-up for those staged by CT was 12.4 years, compared to 4.9 years for those staged by PET. DFS was better for those staged with CT compared to PET, but this difference did not reach statistical significance (88% vs 68% at 5 years, respectively, p=0.14). Twelve pts received 4 doses of adjuvant Rituximab following IFRT; significantly more of these pts were Stage II compared to those who did not receive upfront Rituxan (50% versus 9%, respectively, p=0.007). With a median follow-up of 5.2 years, DFS was significantly worse in Rituxan treated pts compared to those who did not receive Rituxan (5 year DFS of 45% vs 87%, respectively, p=0.04).

Conclusions: In this retrospective analysis of low-grade limited stage NHL pts treated with initial radiation, a significant difference in DFS based on staging by CT versus PET was not detected. However, a larger percentage of pts staged by PET were Stage II compared to those staged by CT, a potential confounder. The addition of Rituxan to IFRT in this group of pts yielded worse DFS, although this likely reflects a selection bias of higher stage patients in this retrospective study. A randomized controlled trial of IFRT with or without Rituxan, stratified by Stage, is needed to establish the role of Rituxan in this patient population.

423 WITHDRAWN

424 PROGNOSTIC SIGNIFICANCE OF RESPONSE QUALITY (RQ) IN PREVIOUSLY UNTREATED FOLLICULAR LYMPHOMA (FL) PATIENTS TREATED WITH COMBINATION RITUXIMAB, CYCLOPHOSPHAMIDE, VINCRISTINE AND PREDNISOLONE (R-CVP)

J. Okosun[1], A. Mwirigi[2], C. Kyriakou[3], K. Cwynarski[1], D. Hughes[1], P. Fields[2], C. Mcnamara[1]
[1]Haematology, Royal Free Hospital, London, United Kingdom, [2]Haematology, Guy's and St Thomas' Hospital, London, United Kingdom, [3]Haematology, Northwick Park Hospital, London, United Kingdom

Introduction: The relationship between RQ and survival in FL is controversial; effective therapies with high response rates have failed to demonstrate consistently better outcomes than less effective therapies. However, a recent study that included a proportion of rituximab treated patients demonstrated an association between RQ and overall survival (OS). Currently, no studies using other R-chemotherapy strategies have investigated this relationship. We report on the effect of response quality on survival following chemotherapy with R-CVP, the most commonly used regimen for FL in the UK.

Patients and Methods: We retrospectively analysed the data of 52 previously untreated patients with FL treated with R-CVP from 4 UK centres. All patients had conventional criteria mandating therapy. Response was assessed according to the revised Cheson criteria. We then examined the relationship between RQ (CR vs PR) with both progression free survival (PFS) and OS. Survival curves were calculated using the Kaplan Meier method.

Results: At the time of therapy, the median age was 64 (range 32-86; 15 M: 35 F). The majority (88%) had advanced stage disease; the remainder had bulky stage II disease. Half (52%) had bone marrow involvement. The Follicular lymphoma international prognostic index (FLIPI) distributed our patient cohort into low (16%), intermediate (42%) and high (42%) risk. Median number of cycles administered was 6 (range 3-8). Median follow-up period was 37.5 months (range 8-117).

Of 50 evaluable patients, 19 (38%) achieved CR, 29 (58%) PR and 2 (4%) had stable disease. Of the responders, 16 out of 48 (33%) patients progressed (4 patients in CR, 12 patients in PR). Those achieving CR had improved progression free survival (PFS) compared with those achieving PR (5 yr PFS 68% vs 44%, p = 0.05). The 5-yr OS in those with CR was 87% and 77% in those with PR respectively (p = 0.22). Three patients had high grade transformation all of which had achieved PR previously.

Conclusions: Our findings suggest a relationship between RQ and PFS for R-CVP treated patients. Interpretation of OS may be limited by the low event rate in the CR group (1 patient death). We suggest that our findings confirm the importance of obtaining a CR during initial therapy for symptomatic FL and have implications for trial design as there are now therapeutic options to improve response quality at the end of induction therapy e.g. maintenance rituximab and radioimmunotherapy.

425 WITHDRAWN

426 HIGH IPI AT RECURRENCE PREDICTS POOR PROGNOSIS AND TRANSFORMATION ON RELAPSED FOLLICULAR LYMPHOMA PATIENTS IN RITUXIMAB-ERA

K. Nakano[1], E. Nara[1], K. Nasu[1], K. Suzuki[1], K. Ueda[1], N. Nishimura[1], Y. Mishima[1], S. Sakajiri[1], M. Yokoyama[1], Y. Terui[1], S. Takahashi[1], N. Tsuyama[2], K. Takeuchi[2]
[1]Hematology / Medical Oncology, The Cancer Institute Hospital of JFCR, Tokyo, Japan, [2]Pathology, The Cancer Institute, Tokyo, Japan

In rituximab era, prognosis of follicular lymphoma (FL) patients has been improving but FL is difficult to cure even now. Almost FL patients relapse again in their long clinical courses and prognosis will be poor in case transformation occurred. We already have some indices for evaluating risk of FL patients such as IPI, FLIPI and FLIPI2. Once FL patients relapse, however, what clinical status suggest good or poor prognosis in not clear. We need good indices for evaluating prognosis of FL patients at recurrence for deciding salvage therapy, as at diagnosis.

We retrospectively reviewed 182 FL patients diagnosed and treated in our institute from April 1997 to January 2009. Of them, 67 patients relapsed once or more in their clinical courses and we evaluated their prognosis. Clinical data at diagnosis and at recurrence were collected and assessed for association of transformation. We also estimated risk of poor prognosis from clinical status at recurrence.

Median follow up time from diagnosis was 59.4 months (range 7.6-154.8) and time to progression from first line therapy was 29.1 months (range 1.0-106.7). Fifty patients (74.6 %) received rituximab-containing chemotherapy as first-line therapy. At recurrence re-biopsy was performed in 45 patients (67.2 %) and 15 patients proved to be transformed pathologically. Two-year overall survival rate from first relapse was 82.2 %. Univariate analysis revealed high serum CRP, IPI at recurrence and FLIPI at recurrence were associated to transformation (P value 0.030, 0.007 and 0.021, respectively), but only high IPI (3 or more) was significant independent predictive factor for transformation by multivariate logistic regression analysis (odds ratio 8.361, P value 0.003).

For relapsed FL patients in rituximab-era, IPI at recurrence is useful index for predicting transformation and poor prognosis.

427 RISK FACTORS IN FIRST RELAPSE OF FOLLICULAR LYMPHOMA

B. Andjelic[1], B. Mihaljevic[1], D. Antic[1], M. Todorovic[1]
[1]Department for Hodgkin's Lymphoma and Hematological Malignancies of Mature B, T and NK cells, Clinic for Hematology, Clinical Center of Serbia, Belgrade, Serbia and Montenegro

Background: The outcome of follicular lymphoma (FL) patients significantly improved during the past few years, after adding of rituximab to standard chemotherapy. Despite to this progress, there are still patients who have bad clinical course, characterized by numerous and frequent relapses, with short survival as the consequence. This heterogeneity in clinical course is even more expressed in relapse. FLIPI is widely accepted index for risk stratification of newly diagnosed FL patients. In relapse of the disease, the adequate prognostic model is still not developed.

Material and Methods: The retrospective analysis was performed on 60 patients treated on Clinic for Hematology, Clinical Center of Serbia, with diagnosed first relapse of FL grade I, II or IIIa, in the period February 2002-April 2009. The patients were initially treated with R±CHOP or R±CVP. In first relapse they were treated with fludarabine based regimens, 33 patients received immunochemotherapy (R-FC, R-FMD) and 27 chemotherapy (FC, FMD). The patient and disease characteristics in first relapse examined as possible risk factors were age, sex, hystological grade, early relapse (in 12 months after first remission), Ann Arbor Clinical Stage, bone marrow infiltration, presence of B symptoms, presence of "bulky" tumor (>10 cm in diameter), ECOG performance status, spleen enlargement, FLIPI score, hemoglobin level, LDH and ESR.

Results: The median follow up was 26 months (range 4-97 months). The survival analysis indicated shorter overall survival in males (log rank=5.656, p<0.05), in patients with hystological grade IIIa (log rank=9.899, p<0.01), in early relapsed patients (log rank=4.692, p<0.05), in patients with B symptoms (log rank=12.752, p<0.01), ECOG performance status>1 (log rank=25.894, p<0.01), Hb<120 g/l (log rank=6.329, p<0.05), ESR> 30 mm/h (log rank=7.121, p<0.01), FLIPI high risk (log rank=9.349, p<0.01) and in patients treated with chemotherapy (log rank=8.234, p<0.01). In multivariate Cox regression analysis ECOG>1, FLIPI high risk and chemotherapy as a treatment option were identified as independent prognostic factors for poor outcome.

Conclusion: FLIPI prognostic score is also useful predictor for outcome in first relapse of FL. Studies with large series of patients treated with immunochemotherapy in relapsed FL seems to be needed, in order to identify patients who maybe require more aggressive therapeutic approach.

428 BENDAMUSTINE TREATMENT FOR NON-HODGKIN LYMPHOMA (NHL) AND CHRONIC LYMPHOCYTIC LEUKEMIA (CLL): CLINICAL EXPERIENCE OF THE SPANISH REGISTRY

B. Sanchez-Gonzalez[1], F. J. Peñalver[2], A. Medina[3], H. Guillen[4], M. Calleja[4], M. Gironella[5], R. Arranz[6], E. Sebastian[7], R. Oña[8], A. Salar[1]
[1]Hematology, Hospital del Mar, Barcelona, Spain, [2]Hematology, Hospital de Alcorcon, Madrid, Spain, [3]Hematology, Hospital Costa del Sol, Marbella, Spain, [4]Hematology, Hospital Principe de Asturias, Madrid, Spain, [5]Hematology, Hospital Vall d'Hebron, Barcelona, Spain, [6]Hematology, Hospital la Princesa, Madrid, Spain, [7]Hematology, Hospital Universitario de Salamanca, Barcelona, Spain, [8]Hematology-BMT Unit, MD Anderson International, Madrid, Spain

Introduction: Bendamustine (B) is a purine analog/alkylator hybrid with antitumor activity. B is currently licensed by EMEA for use in NHL, CLL and multiple myeloma. Our aim was to analyze retrospectively the efficacy and toxicity of B for NHL and CLL in Spain.

Patients and Methods: From June 2009 to September 2010, a questionnaire form was sent to Spanish centers in which B had been used as Compassionate Use Program. Patients with relapsed or refractory NHL or CLL after at least 1 prior treatment regimen were eligible. Any B regimen was included.

Results: 109 patients (pts) were included from 22 institutions. Histology: 42 pts CLL; 18 pts aggressive NHL; 49 pts indolent NHL. Median time from diagnosis to B treatment was 4.9 years (range 1-24). Median number of previous treatment regimens was 3 (range 1-11). 44 pts (40%) were refractory to prior treatment. The most frequent used regimen was rituximab plus B (RB) independently of the histology. 63% of the pts had adverse events grade III/IV (mainly hematology toxicity). Overall response rate (ORR) was 66% (30% complete response (CR)). Response rate was higher in mantle cell lymphoma (86%). ORR observed in refractory pts was 45%, including fludarabine resistant pts. The median progression-free survival (PFS) was 12.7 months (95% CI%, 7.14 to 18.23). Among follicular NHL and CLL pts, median PFS time was 12.4 vs 8.9 months, respectively. The factors significantly affecting PFS were number of treatments prior to B (except follicular NHL), resistance to prior chemotherapy and type of response achieved to B therapy.

Conclusions: 1. Bendamustine containing therapy achieved a high response rate in this heavily pretreated CLL and NHL pts with an acceptable toxicity profile. Responses were seen in indolent and aggressive histology, and also in patients with chemoresistant disease to previous regimen. 2. Histology and number of prior treatment were the most important factors affecting PFS.

429 ECONOMIC IMPACT OF RITUXIMAB AS MAINTENANCE THERAPY IN PREVIOUSLY UNTREATED FOLLICULAR NON-HODGKIN'S LYMPHOMA IN THE US

C. Reyes[1], M. Friedmann[2], L. Han[2], R. Chien[2], R. Hornberger[2], S. Satram-Hoang[1], J. Hornberger[2]

[1]Health Outcomes and Payer Support, Genentech, Inc, South San Francisco, United States, [2]Health Economics, Cedar Associates, LLC, Menlo Par, United States,

Background: Maintenance rituximab (R) therapy every two months for 2 years after chemoimmunotherapy (R-Chemo) has demonstrated improved progression-free survival (PFS) in previously untreated follicular lymphoma (f-NHL), but its economic implications are yet to be determined. A cost-effectiveness analysis (CEA) and budget-impact analysis (BIA) of R-maintenance versus observation was conducted from a typical US payer perspective.

Methods: Treatment-effect assumptions were obtained from the PRIMA trial. We developed a Markov model to project PFS and overall survival (OS) data over a lifetime horizon. Costs calculated in 2010 US dollars included chemotherapy drugs, administration, treatment of grade 3/4 adverse events, and subsequent therapies after disease progression. Drug costs were based on average trial dose and were calculated using CMS fee schedules and wholesale acquisition costs. Utilities for stable and progressed disease were obtained from the literature. Primary endpoints were (1) cost per quality-adjusted life year (QALY) gained and (2) incremental payer budget divided by number of health plan members, referred to as cost per member per month (PMPM). Sensitivity analyses were conducted to identify cost drivers and to quantify the impact of input variables on the outcomes.

Results: Compared with observation, R-maintenance increased mean PFS by 1.53 to 2.55 years and OS by 1.19 to 1.88 years. Acquisition cost of chemotherapy was $48,975.Cost per QALY gained varied between $16,904 and $35,405, depending on the duration of R-maintenance's relative risk reduction of progression. R-maintenance increased the cost PMPM by $0.004. Influential drivers of the BIA were the number of f-NHL patients receiving chemo-induction therapy, the number of patients thereafter receiving R-maintenance, and the cost of R-maintenance.

Conclusion: The use of R-maintenance therapy for previously untreated f-NHL is acceptably cost-effective for oncology with minimal budgetary impact for a typical US health plan.