

[P0208] SAFETY AND EFFICACY OF BENDAMUSTINE THERAPY IN WALDENSTROM MACROGLOBULINEMIA

G Benevolo¹, C Lobetti-Bodoni², L Orsucci¹, B Botto¹, A Chiappella¹, P Riccomagno¹, C Ciochetto¹, R Bruna², L Bergui², M Ladetto², U Vitolo¹. ¹Haematology 2 AUO san Giovanni Battista, Turin, Italy; ²Haematology 1 AUO San Giovanni Battista, Turin, Italy

Background and Aims. Waldenstrom Macroglobulinemia (WM) is a rare low-grade lymphoma characterized by the presence of lymphoplasmacytic cells in the bone marrow and monoclonal IgM in peripheral blood. Bendamustine is a bifunctional alkylating agent that is approved for treatment of lymphocytic leukaemia and indolent non-Hodgkin's lymphomas. So far few data are available on its role in WM. Aim of the study was to test the efficacy and safety of Bendamustine+/- Rituximab therapy in untreated or relapsed WM referred to our institution. *Methods.* A retrospective analysis was performed on 15 WM patients who received therapy with Bendamustine from June 2009 to November 2011 in a single Italian Centre. Eleven patients were male, median age was 74 years (58-81) and all patients had stage IV disease. Based on the Morel ISS-WM study, 3 (20%) patients were high risk, 4 (27%) were intermediate risk, and 8 (53%) were low risk. Six patients received Bendamustine at diagnosis, while 9 patients as second or subsequent lines of treatment (2 in second, 3 in third, 4 patients >3 previous lines respectively). Bendamustine was administered at the standard dose of 90 mg/mq day 1-2 every 28 days in 11 patients, whereas four patients received a dose reduction of 70 mg/mq. Only two patients didn't receive Rituximab due to refractory disease. Median number of delivered cycles was 4 (2-6). *Results.* After a median follow up of 10 months (2-31), 13 patients were eligible for efficacy analysis (two patients are still on therapy). The ORR was 92%. We observed eleven (85%) partial response (PR), one complete response (CR) and one stable disease (SD). CR was obtained in one patient with low-risk ISS treated at diagnosis. We observed a reduction of M protein >50% in 11/13 (85%) patients, whereas in 7/13 (54%) we obtained a reduction of M protein >75%. Moreover, a reduction of >50% of adenopathies and splenomegaly was showed in 12/13 (92%) patients. The therapy with Bendamustine was well tolerated with a low incidence of adverse events, mainly of G1. Three patients developed a G1 or more neutropenia and one of them interrupted therapy for prolonged G4 neutropenia. Three patients were treated with G-CSF. Two pts developed G2 thrombocytopenia. No patients developed a ≥G3 thrombocytopenia. The most common non-haematological adverse events were G1 fatigue (one patient) and infections (two exacerbation of herpes zoster infection requiring treatment were described). *Conclusion.* In our retrospective analysis therapy with Bendamustine+/- Rituximab was well tolerated and effective for WM patients both at diagnosis and at progression. Based on these observations, larger prospective studies to evaluate the role of Bendamustine plus Rituximab in WM patients are warranted.

[P0253] BENDAMUSTINE IN RELAPSED/REFRACTORY MANTLE CELL LYMPHOMA: RETROSPECTIVE ANALYSIS OF THE SPANISH EXPERIENCE

A Garcia-Noblejas¹, B Navarro Matilla², T Gonzalez Lopez³, C Da Silva Rodriguez⁴, JJ Sanchez Blanco⁵, MJ Ramirez Sanchez⁶, C Nicolas⁷, R Perez Fernandez⁸, B Sanchez Gonzalez⁹, E Domingo Domenech¹⁰, C Panizo¹¹, S Macia¹², E Fernandez Fonseca¹³, J

Cannata-Ortiz¹, R Oña Navarrete¹⁴, R Arranz Saez¹. ¹La Princesa University Hospital, Madrid, Spain; ²Puerta de Hierro-Majadahonda University Hospital, Madrid, Spain; ³General Yagüe Hospital, Burgos, Spain; ⁴12 de Octubre University Hospital, Madrid, Spain; ⁵Morales Meseguer University Hospital, Murcia, Spain; ⁶Jerez General Hospital, Jerez, Spain; ⁷Central de Asturias University Hospital, Oviedo, Spain; ⁸Gregorio Marañón University Hospital, Madrid, Spain; ⁹Del Mar Hospital, Barcelona, Spain; ¹⁰Catalan Oncology Institute, Barcelona, Spain; ¹¹Navarra University Clinic, Pamplona, Spain; ¹²Elda Hospital, Elda, Spain; ¹³Rio Ortega University Hospital, Valladolid, Spain; ¹⁴MD Anderson Cancer Center Madrid, Madrid, Spain

Introduction. Patients with Mantle cell lymphoma (MCL) have an adverse outcome after relapse due to refractory disease with conventional treatments. Bendamustine (B), a nitrogen mustard compound chemically related to alkylating agents, has demonstrated high efficacy with a low toxicity profile in reported clinical trials. *Aim.* To analyze the Spanish experience in patients with relapsed/refractory MCL treated with Bendamustine. *Methods.* Retrospective analysis of Spanish experience using Bendamustine alone or in combination in the relapse setting. This study was approved by local ethical committees. *Results.* Forty-three patients have been registered from May to December 2011. *Patient's characteristics.* 67% male, median age 65 years old (range 41-88), 77% ECOG ≤1, 77% Ann Arbor stage IV, 35% high risk MIPI and 12% blastic variant. Previous regimens were CHOP or CHOP like ± R in 41.5%, HyperCVAD/MtxAraC ± R in 39%, R-CVP in 10% and other regimens in 9.5%. Median number of previous treatments were 2.5 (range 1-6), 93% patients had received prior Rituximab and 73% had chemosensitive disease to the last treatment. Bendamustine regimen was R-B (R-375mg/m² D1, B-90 mg/m² D1-2) in 74% patients, R-B with B-70 mg/m² in 9%, B alone in 5%, R-B-Bortezomib in 2% and R-B plus consolidation with stem cell transplant or Y⁹⁰Ibritumomab-tiuxetan in 9%. Median number of cycles was 4.62 (range 1-8). G-CSF support was administered in 46% of cycles. *Response.* Overall response rate was 80%, with 46% CR & uCR and 34% PR. *Survival:* Median progression free survival (PFS) was 18 months (95% CI: 7.6-28.4), data that compares favourably with patient's PFS to previous therapy (12 months, 95% CI: 9.4-14.5). Median PFS for patients who achieved CR/uCR was 35.9 months (95% CI: 19.3-52.7) versus 8.4 months in patients with PR (95% CI: 4.7-12.2). With a median follow-up for surviving patients of 14 months since Bendamustine treatment, the estimated OS at 3 years is 48% (+SD 11%). In the whole series median overall survival from diagnosis is 11.8 years (range: 5.3-18.3 years) without plateau. *Toxicity:* No treatment related mortality has been described. Over 194 cycles, there were 9 hospitalizations due to febrile neutropenia. No tumoral lysis syndrome has been reported. *Conclusions.* Our results with Bendamustine, alone or in combination, confirm the efficacy of this agent in the treatment of MCL, even in the setting of unselected patients previously exposed to multiple therapies including Rituximab.

[P1716] EFFECTIVITY AND SAFETY OF BENDAMUSTINE-RITUXIMAB IN AGED PATIENTS WITH RELAPSED OR REFRACTORY LYMPHOMA

A Cánovas¹, G Barreiro¹, JJ Alonso¹. ¹Hospital Universitario de Cruces, Bilbao, Spain

Background. Bendamustine is a drug with alkylating and antimetabolite properties, with proved activity in relapsed or refractory indolent lymphomas in association with Rituximab. Because of its only moderate toxicity can be safely applied in elderly patients. *Aims.* We present our

experience on treating relapsed or refractory low-grade lymphomas and mantle cell lymphomas with the combination of bendamustine and rituximab (BR). *Patients and Methods.* Prospective and observational study of all consecutive patients with relapsed or refractory low-grade lymphoma or mantle cell lymphoma treated with BR since April the 24th 2008 to January 31st 2012. Informed consent was obtained in every patient. Modified Cheson criteria (2007) were used to assess response. Adverse effects were classified using the WHO toxicity criteria. Bendamustine (90mg/m² daily) was administered the first and second days of each cycle. Rituximab (375mg/m²) was administered a week before the first cycle, the first day of every cycle and four weeks after the last one. Cycles were administered every four weeks to a maximum of six. Patients were evaluable for response if they have received at least two cycles of BR. *Statistical Methods.* Student t, Fisher exact test, Kaplan-Meier tables, log-rank test, Cox multivariate binary logistic and proportional hazard regression. *Results.* Twenty patients were included, 10 females. Mean age: 70 years (44-85); 55% of them were older than 70 years. Diagnosis was follicular lymphoma (FL) in twelve patients, mantle cell lymphoma (MCL) in three, small cell lymphocytic lymphoma (SCLL) in two, lymphoplasmacytic lymphoma (LPL) in two and MALT lymphoma in one. Seventeen patients had relapsed disease and three were refractory to previous treatment schedules. Mean time from diagnosis was 5,5 years (2,6-13,3). Mean number of previous therapies was 3 (1-5), and two patients (one FL and one MCL) have undergone an ASCT. The median number of cycles administered was 4 (mean 4,3; 1-6). Complete response (CR) was achieved in 14 patients (70%) and partial response in 2 (10%). Three patients (15%) showed no response and one was not assessable. None of prognostic variables analyzed (age, sex, functional status, lymphoma type, number of previous treatment and time from diagnosis) was significantly associated with response or toxicity. The median time to treatment failure (TTF) was 19,2 months. Median survival (SV) from the BR treatment onset was 25 months (median observation of live patient: 14,4 months). We analyzed prognostic variables in relation to TTF and SV and none was significant. Adverse events were grade 3 or 4 neutropenia in seven patients (35%) and grade 3 or 4 thrombocytopenia in four (20%). An episode of febrile neutropenia and another of coagulase negative staphylococcus bacteriemia associated with indwelling catheter were reported. There was one hepatitis C reactivation. *Summary/Conclusions.* Treatment with BR was effective in a high percentage of our patients with relapsed or refractory low-grade lymphoma. Of note, tolerability and safety were good and the probability of response and its durability was independent of age. This results confirm the effectiveness of B/R in elderly patients.