[P1669] BENDAMUSTINE IN THE TREATMENT OF AGGRESSIVE NON HODGKIN LYMPHOMA. A RETROSPECTIVE ANALYSIS IN SPAIN

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Introduction. Bendamustine is an alkylating-purine analog hybrid agent currently approved in EU for indolent non Hodgkin lymphoma, chronic lymphocytic leukemia and multiple myeloma; however the experience in aggressive lymphoma is limited. *Aims*. The aim of this study is to evaluate the efficacy and toxicity of Bendamustine in patients with aggressive lymphoma. *Methods*. We conducted a retrospective study to analyze the experience in Spain with Bendamustine alone or in combination in patients with aggressive lymphoma. Nine Spanish hospitals have participated in this study. Endpoints were overall response and complete response rate as *IWRv2003 criteria* and toxicity as *CTCAE v3.0 of NCI scale. Results*. Between August 2009 and December 2011 a total of 30 patients with aggressive lymphoma were treated with Bendamustine in nine medical Institutions in Spain. Male/female: 16/14. Median age 76.6 year (48-88). The histology subtypes were: DLBCL (23) T cell lymphoma (2) and other histology (5). Ann Arbor stage ≥3: 25 cases with extranodal involvement in 22. ECOG ≥2: 13 patients. Bendamustine treatment: 25 patients received Bendamustine as salvage therapy (relapse after CR 12 patients, NR or PR to previous line 13 patients), median of previous lines 3 (1-6). The other 5 patients received Bendamustine as frontline therapy. All patients received a 2 days schedule every 28 days; the most frequent Bendamustine dose/day was 90 mg/m2/day dose (80%). Combined treatment with Rituximab occurred in 84% cases. Median number of cycles: 4 (1-8). Response and outcome: A total of 28 patients completed treatment and were eligible for effectiveness assessment. The overall response rate was 56% (CR 23%; uCR 7%; PR 26%).At the time of reporting with a mean follow up of 20.1 months 19 patients are alive and 7 in CR. All cases of death were progression related. Regarding toxicity, the most common adverse events were hematologic toxicity. Grade 3/4 neutropenia: 10 cases and only 3 episodes of febrile neutropenia. Grade 3/4 anemia: 6 cases. Extra-hematologic toxicity was infrequent and neither dose reduction nor treatment delays, nor hospitalization were influenced by it.No death was attributed to Bendamustine treatment. *Conclusion*. In summary this retrospective study shows that Bendamustine is safe and effective in aggressive lymphoma even in heavily pre-treated patients.

[P0214] BENDAMUSTINE IN HEAVILY TREATED HODGKIN LYMPHOMA, A RETROSPECTIVE FRENCH STUDY IN 28 PATIENTS

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Background. Hodgkin lymphoma (HL) is a curable disease in up to 80% of patients but for the remaining relapsed or refractory (rel/ref) patients no standard salvage therapy exists. Thus new chemotherapeutic agents are needed for HL in relapse following autologous stem cell transplant (ASCT). Bendamustine is a bifunctional alkylating agent, recently FDA approved for the treatment of chronic lymphocytic leukemia and indolent B-cell non-Hodgkin lymphoma. Limited data supports the use of bendamustine in HL (Borchmann, et al. Ann Oncol 1998). *Aims.* This retrospective study evaluate the activity of single-agent bendamustine in rel/ref HL for ASCT failures, non myeloablative transplant (NMT) failures, or patients (pts) who are ineligible for transplant. Our primary outcomes are response rate, toxicity and, progression free survival (PFS) (calculated from the first dose to progression). *Patients and Methods*. From July 2009 to july 2011, 28 patients (16M/12F) with a median age of 25 years (18 -64y) received at least one dose of bendamustine in 7 french centers. First line chemotherapy was ABVD in 25 cases and 12 patients were primary refractory to ABVD and 7 patients received radiation therapy. The median number of previous chemotherapy lines was at 5 (4 - 8) and 4 patients never received ASCT because of no response, 24 received ASCT (tandem autotransplant in 9 cases) and 6 NMT before treatment with Bendamustine. Before the first dose of bendamustine 17/28 patients were "on" chemotherapy and all had platelet counts over 150 G/l. Bendamustine was given for 2 days at 120 mg/m^2 in 8 patients and 90 or 100 mg/m^2 in the remainings, it was associated with rituximab in4 pts, vinorelbine in one pt. *Results.* Two patients received only one course of Bendamustine for grade 4 thrombopénia (bone marrow involvement in one pt) and died rapidly from progressive disease.7 ptsreceived 1-2 cycles,10 ptsreceived 3-4 cycles,9 ptsreceived 5-6 cycles and2 ptsreceived 8 & 12 cycles. 5 patients experienced at least one grade 4 thrombopenia and G-CSF was used in 5 patients. The maximal response (evaluated with PET in 13 cases) was CR/CRu in9 ptsand 6 PR with an overall response rate of 53%. The median PFS was at 8 months (range 1 -18 +) and three patients received subsequent consolidation (REVLIMID n = 1 Chlorambucil n = 1 & NMT n = 1). At the stopping date(December 2011), 10 patients had died from the disease. *Conclusion*. Bendamustine is effective in this heavily pretreated group of patients (mostly end-stage HL) even if the PFS is short. An earlier use should be explored in rel/ref HL, most likely in combination with other drugs such as liposomal doxorubicine or brentuximab vedotine.

[P0782] RITUXIMAB, BENDAMUSTINE AND LENALIDOMIDE IN PATIENTS WITH AGGRESSIVE B-CELL LYMPHOMA NOT ELIGIBLE FOR HIGH DOSE CHEMOTHERAPY OR ANTHRACYCLINE-BASED THERAPY – PHASE I RESULTS OF TRIAL SAKK 38/08

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Background. The majority of patients (pts) with aggressive B-cell lymphoma can be cured with

R-CHOP-like standard first-line therapy. No standard therapy is established for pts who relapsed and are not eligible for intensive salvage regimens including high dose chemotherapy (HDT). In addition, frail pts are often not eligible for first-line anthracycline-based regimens. The combination of rituximab and bendamustine (RB) has demonstrated promising activity and tolerability anti-lymphoma treatment regimen. The immunomodulatory agent lenalidomide has also been shown to be active in the treatment of aggressive B-cell lymphoma. *Aims*. Based on the rationale of a hypothesised synergistic effect of lenalidomide in combination with the RB-regimen, this trial aims to develop a new effective and well tolerated regimen for pts with aggressive B-cell lymphoma not eligible for anthracycline-based chemotherapy or HDT. *Methods*. The phase I part was designed to identify the recommended dose (RD). The tentative RD was defined as one level below the dose level (DL) identifying ≥2/6 pts with a dose-limiting toxicity (DLT) during the first cycle. Lenalidomide was given at 10, 15 or 20 mg (dose level 1 to 3) on days 1-21 in combination with bendamustine 70 mg/m^2 days 1&2 and rituximab 375 mg/m^2 on day 1. Courses were repeated every 4 weeks. DLT was defined as one of the following events occurring within the first cycle: therapy related death, ≥6 missed doses of lenalidomide or delay of > 2 weeks of cycle 2 due to trial drug-related adverse event (AE) toxicity, any grade 3 or 4 non-haematological AE related to trial treatment, neutrophils ≤0.5 x 10^9 G/L for ≥6 days, platelets ≤20 x 10^9 G/L or 21-50 x 10^9 G/L with major bleedings. Informed consent was obtained. *Results*. In the phase I part, 7 pts were enrolled between March 2010 and August 2011. Median age was 77 years (range 67- 79). WHO performance status 0 in 4 pts and 1 in 3 pts; disease stage I: 1 pt, stage II: 2 pts, stage III: 3 pts, stage IV: 1pt; B-symptoms: 2 pts; IPI 1 (2 pts); IPI 2 (4 pts); IPI 3 (1 pt). Two DLTs occurred at DL 2 within the first cycle: 1 pt had a delay of cycle 2 for > 2 weeks due to neutropenia grade 3, 1 pt experienced a grade 4 non-hematologic AE (myocardial infarction). Further non-dose-limiting grade 3/ 4 AE occurred during subsequent cycles: neutropenia grade 3 /4 (2 pts; DL 1), thrombocytopenia grade 3 (1pt; DL 2), febrile neutropenia grade 3 (1pt; DL 2), cardiac arrhythmia grade 3 (1pt; DL 2), gastrointestinal grade 4 (1pt; DL 2), neurologic-sensory grade 3 (1 pt; DL 1), dermatologic/skin grade 3 (1 pt; DL 2). *Conclusion*. The RD for the phase II part has been established at lenalidomide 10 mg/day for day 1-21 in combination with rituximab 375 mg/m^2 day 1 and bendamustine 70 mg/m^2 on day 1&2. Patient accrual is currently ongoing for the phase II part to evaluate the efficacy and safety of this regimen.