Lymphoma - Clinical 1

0270

FRONTLINE TREATMENT WITH THE COMBINATION FLUDARABINE-CYCLOPHOSPHAMIDE IN LOW-GRADE NON-FOLLICULAR NON-HODGKIN LYMPHOMA: A LONG TERM UPDATING OF GISL LL02 TRIAL

A Ferrario,[1] M Goldaniga,[2] F Merli,[3] V Callea,[4] F Ilariucci,[3] C Stelitano,[4] M Russo,[5] P Mazza,[6] S Luminari,[7] L Marcheselli,[7] M Brugiatelli,[8] D Luisi,[9] F Rossi,[2] B Olivero,[2] G Lambertenghi Deliliers,[2] M Federico,[7] L Baldini[2]

[1]UO Ematologia, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Unive, Milano, Italy; [2]UO Ematologia [1], Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Uni, Milano, Italy; [3]Servizio di Ematologia, Arcispedale S. Maria Nuova, Reggio Emilia, Reggio Emilia, Italy; [4]Dipartimento di Ematologia, Azienda Ospedaliera Bianchi-Melacrino-Morelli, Reggi, Reggio Calabria, Italy; [5]UO Ematologia PO San Vincenzo, Taormina, Taormina, Italy; [6]UO Ematologia, AO SS Annunziata, Taranto, Taranto, Italy; [7]Dipartimento di Oncologia e Ematologia, Università degli Studi di Modena e Reggi, Modena, Italy; [8]Divisione di Ematologia, Azienda Ospedaliera Papardo, Messina, Messina, Italy;[9]Dipartimento di Ematologia ed Oncologia, Presidio Ospedaliero, Pescara, Pescara, Italy

Background. Indolent non-follicular lymphomas (NFo-NHL) include small lymphocytic lymphoma (SLL), lymphoplasmacytic lymphoma (LPC), marginal zone lymphoma (MZL). This heterogeneous group show different presenting features, behaviour pattern and treatment outcome. This subset of lymphomas have been relatively poorly investigated, and only retrospective studies or prospective trials involving limited series have so far been published. *Aims.* In 2002 the Gruppo Italiano Studio Linfomi (GISL) initiated LL02 prospective multicenter phase II trial, with the aim to evaluate the efficacy and safety of FC combination as front-line therapy of NFo-NHL patients. *Methods.* Between July 2002 and September 2006, 63 adult patients affected by NFo-NHL in active disease phase, were consecutively enrolled in 12 GISL hematological centres. After histologic revision, 61 patients could be enrolled in the study (36 males and 25 females, median age 64 yrs, range 40-75). The series included 22 cases of SLL, 11 LPC, 25 MZL, 3 CD5 negative NHL cases. Patients were treated with a dose of 25 mg/sqm Fludarabine plus 250 mg/sqm Cyclophosphamide administered intravenously daily for 3 days; each cycle was repeated every 28 days for 6 courses; an intermediate evaluation was performed after the third cycle. During the treatment patients received oral thrimethoprim-sulphametoxazole and fluconazole prophylaxis. *Results.* Two patients were excluded because no further information after registration have been obtained. Six patients were withdrawn before the intermediate evaluation for early toxicity: 2 lethal infective episodes (WHO grade 4), 3 haematological toxicities (WHO grade 3-4) and 1 renal toxicity (WHO grade 4). After the intermediate evaluation, 51/59 patients (86.4%) had an objective response (ORR) with a 22% of complete remission (CR) and 64.4% of partial remission (PR). Among the 53 remaining patients, 43 completed the planned treatment of six cycles, 3 five cycles, 3 four cycles, 2 three cycles and 1 progressed after first cycle. At the final evaluation the ORR percentage was 83% with a 40.6% of CR (24 pts) and 42.3% of PR (25 pts); three patients were in progressive disease (5.0%) and one in stable disease (1.6%). On the basis of intention to treat analysis, after a follow-up of 60 months, the median overall survival (OS) was 64%, the progression free survival (PFS) was 54% and the failure free survival was 39%. The median remission duration was 26 months. After a median follow up of 36 months, mortality was 28% (17/61): among them, it was related to disease relapse/progression (35%), sepsis (29%), second tumor (18%), cerebrovascular event, respiratory insufficiency and other causes (6%). About the toxicity profile, the major toxicity was hematological with a 18% cases of WHO grade III or IV anemia, 34% neutropenia and 11% thrombocytopenia. The 10% of patients had an infective episode of WHO grade III-IV. *Conclusions.* FC chemotherapy is a useful chance for advanced untreated non follicular low-grade NHL, with an optimal ORR, CR and PFS. OS is not significantly improved in comparison with fludarabine alone or with standard therapy, even though the quality of responses was better. Infective (2 early deaths) and haematological toxicity, causing the interruption of the planned treatment in a significant subset of patients, suggest an accurate selection and a careful monitoring during the therapy.

0271

EFFICACY AND SAFETY OF BORTEZOMIB AND RITUXIMAB ASSOCIATION IN RELAPSED/REFRACTORY INDOLENT NON-FOLLICULAR AND MANTLE CELL LYMPHOMA: FINAL RESULTS OF PHASE II STUDY BY INTERGRUPPO ITALIANO LINFOMI

A Chiappella,[1] P Pregno,[1] PL Zinzani,[1] A Evangelista,[2] A Fabbri,[1] F Facchetti,[3] A Ferreri,[1] S Franceschetti,[1] R Freilone,[1] L Gargantini,[1] D Gioia,[1] AM Liberati,[1] L Orsucci,[1] L Rigacci,[1] E Russo,[1] V Stefoni,[1] A Tucci,[1] U Vitolo[1]

[1]On the behalf of Intergruppo Italiano Linfomi (IIL), Torino, Italy; [2]Unit of Cancer Epidemiology, University of Torino and CPO Piemonte, Torino, Italy; [3]Pathology Unit, Spedali Civili Hospital, Brescia, Italy

Background. Bortezomib alone or in combination with Rituximab has shown clinical benefit in treatment of Mantle Cell Lymphoma (MCL) and Marginal Zone Lymphoma (MZL). *Aims.* To evaluate safety and efficacy of Rituximab and Bortezomib combination in relapsed/refractory indolent non-follicular lymphoma and MCL not eligible to high-dose chemotherapy. Patients and *Methods.* The study was a phase II multicenter trial according to Simon's design. Inclusion criteria were: age 18-75 years, histological proven relapsed (> 1 year from the last therapy) or refractory (<1 year) indolent non-follicular (linfocytic lymphoma, LL, or MZL) and MCL after 1-4 lines of therapies. Treatment plan was: one course of four weekly intravenous bolus of 1.6 mg/sqm Bortezomib in combination with four infusion of 375 mg/sqm Rituximab followed by two courses of four weekly bolus of 1.6 mg/sqm Bortezomib. Patients with complete (CR), partial remission (PR) and stable disease at the intermediate evaluation were planned to be given three further courses with the same schedule. *Results.* From September 2006 to March 2008, 55 patients entered into the study. Histology revision was performed by three expert pathologists. Forty-nine patients fulfilled inclusion criteria and were evaluable. Clinical characteristics were: median age 68 (50-74) years; 16 LL, eight MZL, 25 MCL; 42 stage III/IV; 33 bone marrow involvement; 20 at intermediate-high/high IPI risk. Thirty-eigh patients performed > two prior lines of chemotherapy; 34 were Rituximab-pretreated; 21 refractory and 28 relapsed disease. Overall Response Rate (ORR) was 53% (CR 26.5%, PR 26.5%); no response 43% and 4% off therapy for other causes. ORR by histology was: 37% in LL, 50% in MZL and 64% in MCL. ORR was not adversely affected by Rituximab pretreatment: Rituximab-pretreated 62% and Rituximab-naïve 33%. ORR was higher in relapsed patients compared with refractory ones: 64% and 38% (p.06). With a median follow-up of one year, Overall Survival was 89% (95%CI: 75-95) and 1-year Progression free survival (PFS) was 45% (95%CI: 30-58) (Figure 1A). One-year PFS was 50% for MZL and MCL and 37% for LL (Figure 1B).

Figure 1.