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Abstract 2720 Brief Chemoimmunotherapy Rituximab, Bendamustine, Mitoxantrone (R-BM) Followed by Rituximab Consolidation in Elderly Patients with Untreated Advanced Stage Follicular Lymphoma (FL): Preliminary Results of a Prospective Phase II Study by Fondazione Italiana Linfomi (FIL)

Carola Boccomini[1*], Marco Ladetto, MD[2*], Luigi Rigacci[2*], Luca Arcaini[2*], Manuela Ceccarelli[2*], Chiara Lobetti-Bodoni[2*], Stefano Volpetti[2*], Lorella Orsucci[2*], Annalisa Chiarenza[2*], Roberto Freilone[2*], Paolo Corradini[2*], Silvia Bolis[2*], Silvia Franceschetti[2*], Paola Riccomagno[2*], Chiara Rusconi[2*], Alfonso Zaccaria[2*], Caterina Stelitano[2*], Anna Marina Liberati[2*], Chiara Ciochetto[2*], Luca Baldini, MD[2*], Monica Balzarotti, MD[2*], Alessandra Tucci[2*] and Umberto Vitolo[3]

[1]Città della Salute e della Scienza Hospital, Hematology 2, Torino, Italy
[2]On the behalf of FIL
[3]Azienda Ospedaliera Città della Salute e della Scienza di Torino, Hematology 2, Turin, Italy

Introduction: Bendamustine is a promising agent that has been showed high efficacy in combination with Rituximab in indolent lymphomas; however experiences on its use in combination with other cytotoxic agents are scant, particularly in FL. A previous FIL trial showed that a brief R-FND induction chemoimmunotherapy with only 4 courses of R-chemotherapy followed by 4 rituximab doses as consolidation can achieve high CR and PFS rates in FL patients, supporting the feasibility of this regimen in the elderly (Vitolo et al, ASH 2011). These promising results prompted FIL to investigate safety and efficacy of a similar combined brief regimen substituting Bendamustine for Fludarabine aimed at reducing toxicity and maintaining efficacy.

Patients and methods: From September 2009 to November 2011, 76 elderly patients (age 65-80) with advanced stage FL at diagnosis were enrolled. Inclusion criteria were: untreated grade I, II and IIIa FL; advanced disease requiring treatment (stage III/IV) or stage II including at least one of the following conditions: bulky disease (>7 cm), active disease with rapid lymph node progression, lactate dehydrogenase or β2 microglobulin above normal, systemic symptoms and extranodal involvement. A comprehensive geriatric assessment (ADL, I-ADL, CIRS) was also performed at diagnosis and only "FIT" patients were enrolled into the study. Treatment plan was: 4 monthly courses of R-BM (375 mg/m^2

Rituximab day 1, 90 mg/m^2 Bendamustine days 1-2, 8 mg/m^2 Mitoxantrone day 1), followed by consolidation with 4 weekly Rituximab infusions. Polymerase chain reaction (PCR) for BCL2/IgH rearrangement was performed on bone marrow samples at diagnosis, after R-BM and after consolidation.

Results: At the time of analysis, 69/76 patients are evaluable for clinical characteristics, response to treatment and toxicity. Median age was 71 years (range 65-80); 26 males, 43 females; WHO grading was as follow: I 16%, II 55% and IIIa 29%; 19% had advanced stage II disease, 27% stage III and 54% stage IV; 49% had BM involvement, 19% B symptoms and 7% leukemic dissemination; 58% patients had no comorbidity, 20% one and 22% two or more comorbidities. According to FLIPI patients were: 12% at low, 30% at intermediate and 58% at high risk. PCR analysis was carried out in 64 patients at diagnosis: 58% were Bcl-2 positive. Sixty three patients completed the planned treatment and the whole program was completed according to the planned time in 60/63 patients. Six patients did not complete the treatment: 1 for progressive disease, 4 for adverse events (2 haematological toxicity with prolonged neutropenia; 1 CMV colitis and 1 for infection and concomitant worsening of pre-existing oral pemfigo) and 1 patient for worsening of performance status. Overall response after R-BM + Rituximab was observed in 64 (96%) patients with 52 (75%) patients in complete remission and 12 (18%) in partial remission (PR). Response to 4 cycles of R-BM was as follow: 27 (39%) in CR, 37 (54%) in PR and 5 (7%) patients in stable (SD) or progressive disease. Of the 40 patients in PR or SD after 4 R-BM, 26 (65%) converted to CR following further Rituximab consolidation. At the time of this analysis, of the 37 patients Bcl-2 rearranged at diagnosis, 19 (51%) were evaluable for molecular response during and after treatment. PCR negativity was achieved in 16/19 (84%) patients after R-BM and in 18/19 (95%) patients at the end of treatment. A total of 521 courses of R-BM and Rituximab were given. The most frequent severe toxicity (CTC grade 3-4) was neutropenia reported in 18% of the courses; nevertheless only four serious infections were recorded (all due to bacterial agents). Pulmonary and cardiac toxicities were < 1%. Two deaths were recorded: one due to lymphoma after second line treatment and one due to hepatic carcinoma occurred 3 months after completion of therapy.

Conclusions: A brief course of chemo-immunotherapy R-BM followed by Rituximab consolidation is safe and effective with a high CR rate in elderly patients with untreated advanced stage FL. Planned future analysis of the entire study will give further information on late toxicity and outcome.

Disclosures: Off Label Use: In Europe use of Bendamustine in first-line treatment of follicular lymphoma is off-label. Drug was provided free by Mundipharma.. **Vitolo:** *Roche:* Membership on an entity's Board of Directors or advisory committees.

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[*] signifies non-member of ASH