SUPPLEMENTARY APPENDIX

Rituximab plus bendamustine as front-line treatment in frail elderly (>70 years) patients with diffuse large B-cell non-Hodgkin lymphoma: a phase II multicenter study of the *Fondazione Italiana Linfomi*

Sergio Storti,[1] Michele Spina,[2] Emanuela Anna Pesce,[3] Flavia Salvi,[4] Michele Merli,[5] Alessia Ruffini,[6] Giuseppina Cabras,[7] Annalisa Chiappella,[8] Emanuele Angelucci,[9] Alberto Fabbri,[10] Anna Marina Liberati,[11] Monica Tani,[12] Gerardo Musuraca,[13] Annalia Molinari,[14] Maria Pia Petrilli,[1] Carmela Palladino,[4] Rosanna Ciancia,[2] Andrea Ferrario,[5] Cristiana Gasbarrino,[1] Federico Monaco,[4] Vincenzo Fraticelli,[1] Annalisa De Vellis,[1] Francesco Merli[15] and Stefano Luminari[15,16]

[1]Department of Hematology, Universita' Cattolica Sacro Cuore Campobasso; [2]Division of Oncology A, National Cancer Institute Aviano; [3]Fondazione Italiana Linfomi Onlus; [4]Hematology Unit, Antonio e Biagio e Cesare Arrigo Hospital, Alessandria; [5]Department of Hematology, Ospedale di Circolo e Fondazione Macchi - ASST Sette Laghi, Varese; [6]GRADE - Gruppo Amici Dell'Ematologia; [7]Unit of Hematology Ospedale Businco, Cagliari; [8]Department of Hematology, Città della Salute Hospital and University, Torino; [9]Ospedale Policlinico San Martino, Genova; [10]Azienda Ospedaliera Universitaria Senese, U.O.C. Ematologia, Siena; [11]Università degli Studi di Perugia, A.O.S. Maria, Terni; [12]Department of Hematology, S. Maria delle Croci Hospital, Ravenna; [13]Department of Hematology, IRCCS - Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (I.R.S.T.), Meldola; [14]Department of Hematology, Infermi Hospital, Rimini; [15]Department of Hematology, Azienda Unità Sanitaria Locale IRCCS di Reggio Emilia and [16]Department of Clinical Diagnostic and Public Health Medicine, Università degli Studi di Modena e Reggio Emilia, Modena, Italy

 doi:10.3324/haematol.2017.186569

Received: December 20, 2017.

Accepted: May 3, 2018.

Pre-published: May 10, 2018.

Correspondence: stefano.luminari@ausl.re.it

Supplementary Methods.

Patient eligibility

Eligible patients were elderly patients aged ≥ 70 years with a newly diagnosed, histologically proven, DLBCL. As indicated in the manuscript, patient had a FRAIL profile, defined with comprehensive geriatric assessment (CGA) originally reported as part of pre-therapy assessment. All patients had to sign the informed consent form before study enrollment.

A negative serology for hepatitis B, hepatitis C and HIV were required; patients with HBcAb positivity were included but had to receive Lamivudine prophylaxis. Patients with history of other malignancies within 5 years prior to study entry (except for adequately treated carcinoma in situ) or those with Central Nervous System (CNS) involvement by lymphoma, or evidence of any severe active acute or chronic infection were excluded. Patients with any other co-existing medical or psychological condition that could precluded participation in the study or compromised ability to give informed consent or with Concurrent co-morbid medical condition which might exclude administration of full dose chemotherapy, were excluded from the study.

Study procedure

Mandatory baseline assessments included blood counts and biochemistry tests, chest abdomen and pelvis CT scan, electrocardiogram (ECG), bidimensional cardiac assessment of Left Ventricular Ejection Fraction (LVEF). FDG-PET, Bone Marrow Biopsy (BMB) and Bone Marrow Aspirate (BMA) with flow cytometry analysis were optional.

At the end of treatment, blood tests, chest, abdomen and pelvis CT scan, ECG, LVEF assessment, were performed. BMB was recommended if performed at diagnosis with positive result. Total body FDG-PET scan was optional. During the follow up, blood tests and physical examinations were required every three months. Every six months chest x-ray, ECG and cardiac assessment. Chest, abdomen and pelvis CT-scan was performed every year.

Concomitant medication

During treatment, patients could receive prophylaxis with G-CSF, valacyclovir and cotrimoxazole. Prophylaxis with quinolones and antifungals was administered in case of grade 3 neutropenia. Erythropoietin use was allowed according to ASH/ASCO guidelines. In patients HBcAb+, prophylaxis against hepatitis B reactivation with Lamivudine 100 mg/die from the start of the treatment to one year after the end of the treatment were recommended. All concomitant medications for medical conditions other than B-NHL were permitted, as clinically Indicated. All supportive therapies other than anti-cancer treatment needed for the management of patients enrolled in this study were permitted.

Supplementary Table 1. Comorbidities CIRS-G 2 and CIRS-G ¾.

Comorbidity	CIRS-G 2	CIRS-G ¾
	N (%)	N (%)
Cardiac	12 (27)	6 (13)
Hypertension	17 (38)	2 (4)
Vascular	13 (29)	2 (4)
Respiratory	5 (11)	6 (13)
Eye, ear, nose, throat, larynx	9 (20)	0
Upper gastrointestinal	3 (7)	0
Lower gastrointestinal	4 (9)	0
Hepatic	1 (2)	0
Renal	2 (4)	1 (2)
Others (urinary, genitals)	8 (18)	0
Musculo-skeletal	11 (24)	1 (2)
Neurological	8 (18)	2 (4)
Endocrine-metabolic	14 (31)	2 (4)
Psychiatric	10 (22)	0

CIRS-G: Cumulative Illness Rating Scale, geriatric