Protocol Synopsis

Title of the study	Phase II study to confirm the effectiveness of Bendamustine in adjunct to Etoposide, Aracytin and Melphalan (BeEAM) as a preparative regimen for autologous stem cell transplantation in resistant/relapsed Aggressive B-cell non-Hodgkin Lymphoma patients.
Principal Investigator	Giuseppe Visani, MD
EUDRACT code	2011-001246-14
Type and number of subjects	Adult ~~agressive~~aggressive B-cell non-Hodgkin lymphoma patients.
Primary Objective	• To assess the 1-year complete remission (CR) rate.
Secondary Objectives	• To assess the safety of the regimen • To assess the disease-free survival • To assess the overall survival
Study design	Open-label, non-randomized, multicentric, Phase II study
Number of patients and time frame	~~100 patients will be enrolled in 12-18 months~~ 66 patients wil be enrolled
Inclusion Criteria	• Aggressive B-Cell non-Hodgkin lymphoma patients either resistant or relapsed • Age >18 and <70 years • Signed Informed Consent • Karnofsky score > 70% •Adequate hematologic, renal, pulmonary and hepatic function.
Exclusion criteria	• HIV infection •Secondary lymphoma following prior chemotherapy/ radiotherapy or an active second malignancy • Pregnancy or nursing •Absence of patient's written informed consent • Current uncontrolled infections

	•Intercurrent organ damage or medical problems that would interfere with therapy
Criteria for evaluation	Safety: Incidence of adverse events (graded according to WHO) and clinically significant abnormal laboratory value after BeEAM chemotherapy followed by the reinfusion of autologous hematopoietic stem cells Efficacy: Assessment of the percentage of patients entering CR after BeEAM chemotherapy_followed by the reinfusion of autologous hematopoietic stem cells. Disease-free survival. Overall survival.
Chemotherapy Schedule	• Bendamustine 200 mg/m^2 on day -7 and -6 • Aracytin 400 mg/m^2 from day -5 to day -2 • Etoposide 200 mg/m^2 from day -5 to day -2 • Melphalan 140 mg/m^2 on day -1 • Autologous stem cell transplantation on day 0 All patients will be hospitalized during the study treatment, until the complete hematological recovery has occurred.
Statistical analysis	This study is designed according to Fleming's method. The primary outcome is the 1-year Complete Remission Rate. Fixing the lowest acceptable rate as 55% and the successful rate as 70%, with a significance level α=0.05 and a power 1-β =~~0.90~~ 0.80, the sample size was estimated in ~~88~~ 64 patients. Considering a possible drop-out rate of ~~10~~3%, the number of patients entering the protocol is fixed to ~~100~~ 66.