FIL-VERAL12: phase II randomized study with Rituximab-DHAP +/- Bortezomib as induction in young relapsed/refractory Diffuse Large B-cell Lymphoma eligible to transplant.

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On behalf of Fondazione Italiana Linfomi.

BACKGROUND

- The addition of rituximab to CHOP improved prognosis in DLBCL patients.[1]
- The best salvage regimen is not yet established, but a cisplatin-containing regimen (DHAP, cisplatin, high-dose citarabine, dexamethasone) is worldwide accepted as a good option.[2,3]
- R-DHAP showed an activity expecially in non germinal center (non-GCB) derived DLBCL.[4]
- Bortezomib had proven activity in aggressive lymphoma (especially mantle cell lymphoma) subtypes; when combined to DAEPOCH, showed promising activity in non-GCB DLBCL.[5,6]
- A phase III randomised trial conducted on myeloma patients demonstrated that SC bortezomib offers non-inferior efficacy to standard IV administration, with an improved safety profile especially in terms of peripheral neurotoxicity.[7]

METHODS

- This is a prospective, multicenter, two-arm randomized phase II screening trial designed to assess whether the addition of Bortezomib to R-DHAP is more promising than standard R-DHAP as induction therapy before high dose chemotherapy with stem cell transplant in terms of efficacy on an intermediate endpoint (CR) and safety.

KEY INCLUSION CRITERIA

- Relapsed/refractory DLBCL after first line R-CHOP or GA101-CHOP
- Age 18-65 years
- Eligible to high-dose therapy.
- All relapsed patients will be re-biopsied for centrally histological review and classification according to cell of origin profile.

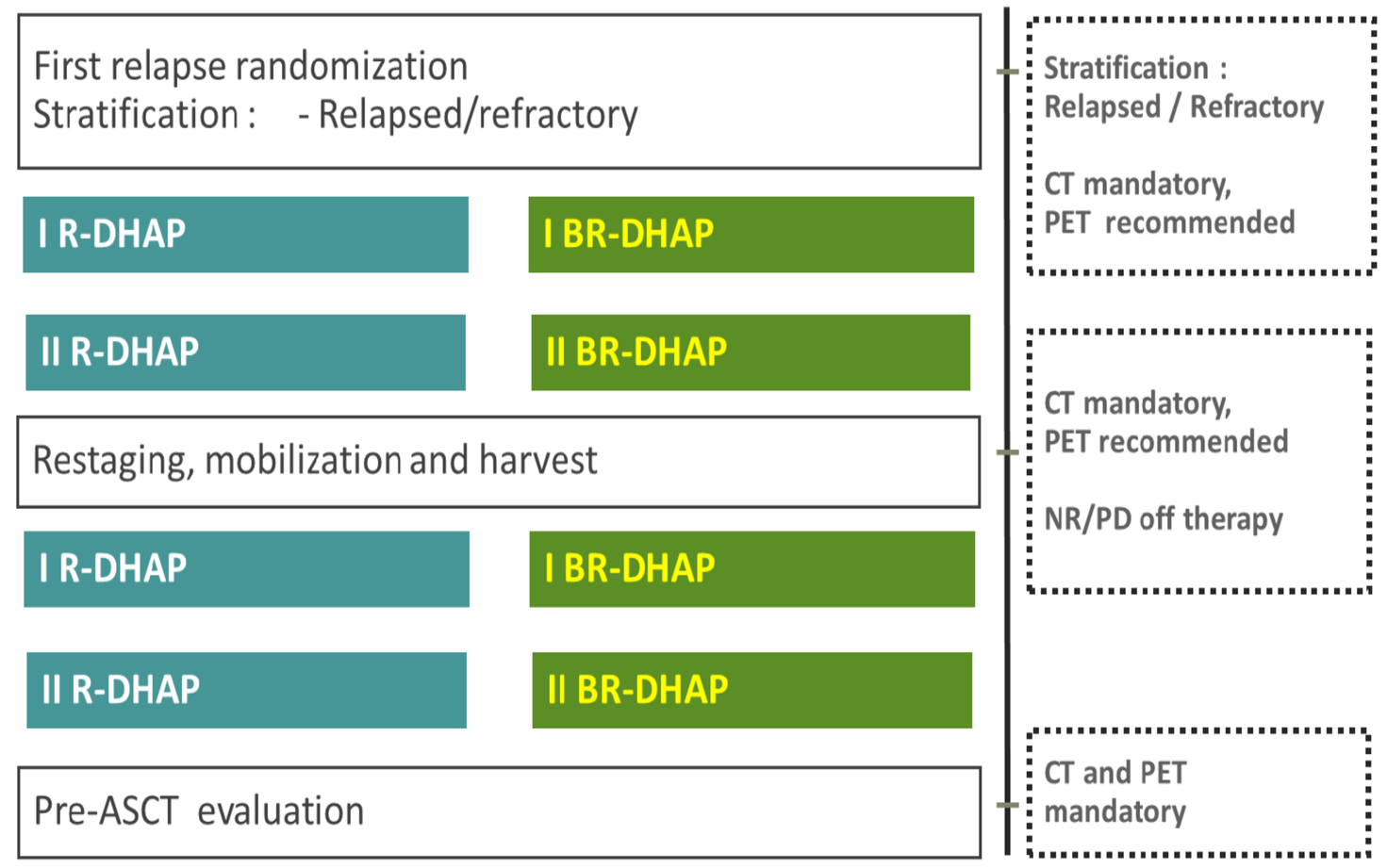
BR-DHAP REGIMEN

- Standard R-DHAP q 28 days outpatient
- Bortezomib sc 1.5 mg/sqm day 1, day 4 (provided free by Janssen-Cilag)

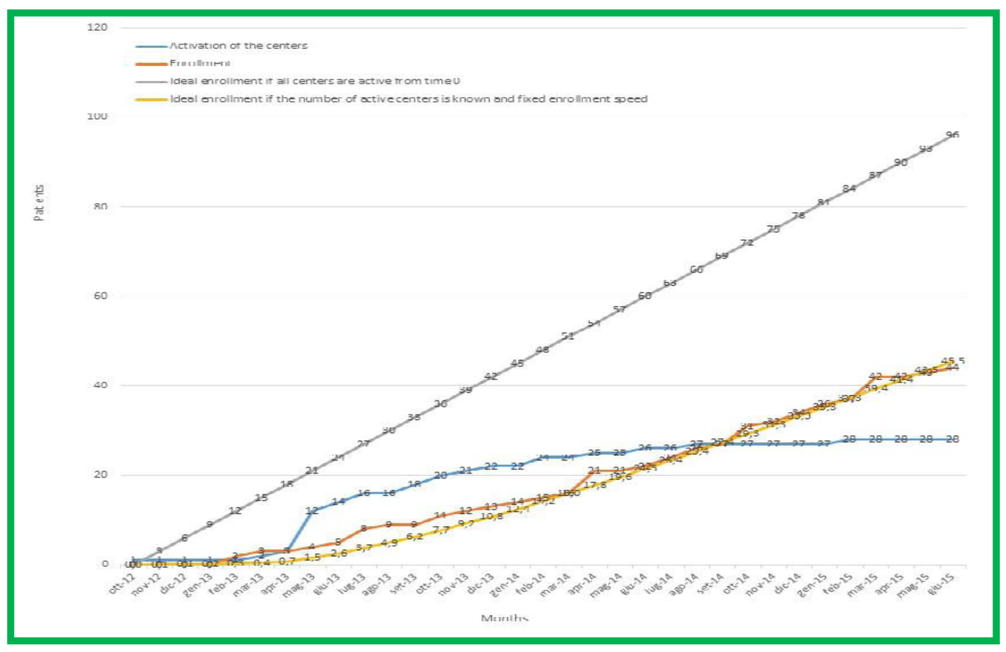
STATISTICAL DESIGN

- Prospective, multicenter, two-arm randomized phase II screening trial
- Randomization (1:1) R-DHAP every 28 days for 4 cycles and Bortezomib-R-DHAP (BR-DHAP); stratification: relapsed/refractory.
- Primary end point: CR (PET negative) at Pre-ASCT evaluation and safety.
- According to a one-sided test with an alpha-error of 0.10 and a beta-error of 0.20, and assuming a 30% CR for the standard arm R-DHAP and an expected CR rate in experimental arm of 50%, a sample size of 108 patients (54 for each arm) is required.

VERAL12 STUDY FLOW



ENROLLMENT STATUS



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