SPLIT-DOSE R-CHOP WITH INTERIM DE-ESCALATION OF THERAPY IN ELDERLY PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA

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Background

Management of DLBCL in older adults (OA) is challenging, requiring a personalized approach that accounts for age associated comorbidities and frailty. Many OA receive non-anthracycline based treatment, or attenuated regimens (i.e. R-miniCHOP) to avoid toxicity. However, DLBCL remains the leading cause of death for OA treated with these regimens. SD R-CHOP is an alternative approach where pts receive CHOP at 50% dose reduction on days 1 and 15 of each 28-day cycle with full dose R on Day 1 for 6 cycles. The cumulative dose of one cycle of SD R-CHOP is equal to one cycle of R-CHOP-21.

Split-Dose R-CHOP Regimen

Day 1 ("A") Cycles	Day 15 ("B") Cycles
Rituximab 375 mg/m^2	Cyclophosphamide 375 mg/m^2
Cyclophosphamide 375 mg/m^2	Adriamycin 25 mg/m^2
Adriamycin 25 mg/m^2	Vincristine 1 mg
Vincristine 1 mg	Prednisone 50 mg x 5 days
Prednisone 50 mg x 5 days	

Growth factor given with both "A" and "B" cycles to minimize neutropenia

Objectives

Determine the end of treatment (EOT) complete response (CR) rate with SD-R-CHOP in elderly DLBCL.

Methods

We conducted a Phase II, prospective study of SD-R-CHOP in elderly DLBCL conducted via the Wisconsin Oncology Network (NCT03943901). Patient population included treatment naïve DLBCL patients aged≥75 years or 70-74 years plus elevated cumulative illness rating scale for geriatrics score were included. Treatment consists of two cycles of SD-R-CHOP followed by interim response assessment with PET/CT and peripheral blood cell-free ClonoSEQ minimal residual disease (MRD) testing (Figure 1). Patients with both Deauville score 1-3 and MRD negativity were offered abbreviated therapy with two additional cycles of SD-R-CHOP. All others completed 6 cycles.

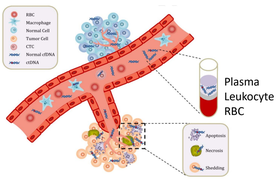
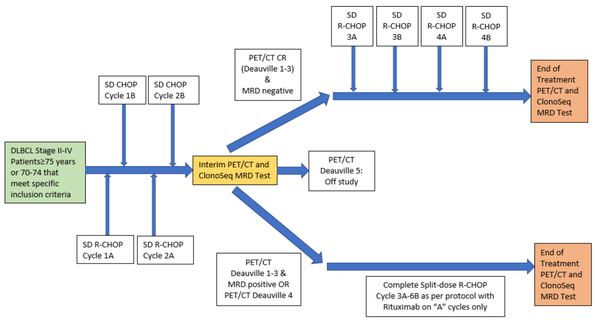


Figure 1: Cell free (cfDNA) originates from cells and is released into the bloodstream through normal cell turnover (eg, apoptosis, necrosis, shedding) Circulating tumor (ctDNA) is released from tumor cells and is a subset of cfDNA. ctDNA is a promising biomarker for tumors which reside within specific sites of the body. For diseases like DLBCL which reside in organs such as lymph nodes, MRD is more readily detected via ctDNA than from cells in the blood

STATISTICAL CONSIDERATIONS: Assuming a baseline CR rate of 50% with target enrollment of 26 patients, if 16+ patients achieved a CR, this treatment would be considered promising.

Split-Dose R-CHOP Treatment Regimen

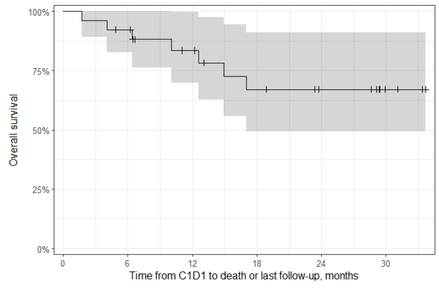


Patient Demographics	n=26 patients
Male Sex	56% (n=12)
Stage III-IV	85% (n=22)
Median age	80 years (range 71-88)
De Novo DLBCL Transformed DLBCL	77% (n=20) 23% (n=6)
"B" Symptoms	35% (n=9)

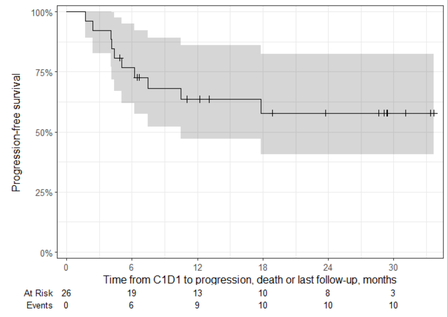
Results

Among 26 treated patients, median age was 80 years (71-88) and most had stage IV disease (58%). The EOT CR rate for all patients was 65% exceeding target threshold. Nine patients (35%) were interim MRD-/PET- after Cycle 2 and 8 of these 9 patients (89%) achieved an EOT CR. 16 patients were assigned to the full treatment arm (6 cycles) and the EOT CR rate was 56%. The 1-year overall survival (OS) was 82% and 1-year progression free survival (PFS) was 67%. Neither median OS nor PFS were reached to date. There were two non-relapse mortality events due to infection and cardiac complications.

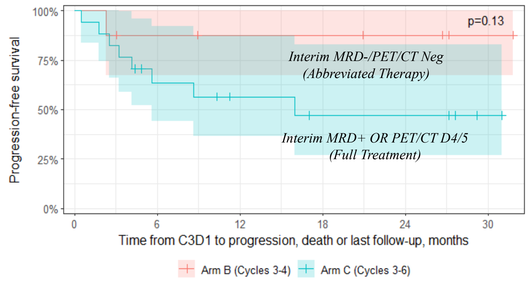
Overall Survival



Progression Free Survival



Progression Free Survival by Treatment Arm



Discussion

SD-R-CHOP offers older DLBCL patients equivalent dose intensity as R-CHOP-21 through a fractionated dosing schedule improving tolerability. The EOT CR rate for all patients was 65% demonstrating the value of maintaining dose intensity for older patients. EOT CR was 89% for interim PET-/MRD- patients despite abbreviated therapy. These data support de-escalation of therapy as a feasible approach for patients with interim PET-/MRD- disease assessment which limits toxicity without impacting long-term outcomes. Lastly, despite escalating cumulative R-CHOP dose to the same dose intensity as younger patients, through fractionation this regimen was well tolerated with expected toxicities consistent with CHOP like chemotherapy.

Acknowledgements

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