Reduced-Intensity Anthracycline-Free Chemoimmunotherapy in Elderly Patients With Newly Diagnosed or Relapsed Diffuse Large B cell Lymphoma (DLBCL)

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INTRODUCTION

Elderly DLBCL patients have suboptimal outcomes due to poor tolerance of anthracycline-containing regimens. We previously reported 5 elderly patients with new or relapsed DLBCL treated with anthracycline-free chemoimmunotherapy (CI). We are updating this report, including longer follow-up and an increase to 8 patients continuing to demonstrate impressive clinical activity.

AIM

To demonstrate the effectiveness and durability of therapeutic responses of an anthracycline-free CI regimen in elderly patients with newly diagnosed or relapsed DLBCL.

METHOD

REGIMEN: Rituximab:375mg/m2 D1.
Cyclophosphamide: 750 mg/m2 D1.
Vincristine: 1.4mg/m2= 2mg D1
Prednisone: 40mg/m2 =100mg by mouth daily X 1-5 days combined with lenalidomide 25 mg by mouth daily for 21 days , followed by 1 week off. (R2-COP).

RESULTS

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age (years)	76	83	79	74	72	87	72
Sex	F	F	M	F	F	M	M
ECOG PS	3	2	4	4	0	2	2
Charlson comorbidity index	5	12	6	6	7	6	6
DLBCL subtype	GCB	GCB	GCB	ABC	GCB	ABC	ABC
Ki-67	60	90	90	95	80	95	80
DEL/DHL/THL	No	No	No	DEL	No	DEL, FISH not available	No
AJCC stage	IVB	IVE	IE	IV	IV	IVB	IV
Albumin(g/dL)	2.9	2.9	3.1	1.5	2.7	2.4	2.6
LDH (U/L)	154	227	213	270	256	627	328
IPI score	3	5	3	4	4	5	4
Extranodal sites	Tonsil, nasopharynx	Liver	Left nostril	Oropharynx	Lung	Lungs, spleen, and bilateral kidneys	Oropharynx
Bone marrow involvement	No	No	No	No	No	No	No

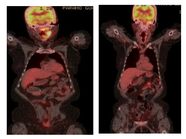
ECOG: Eastern Cooperative Oncology Group; PS: performance status; DLBCL: diffuse large B-cell lymphoma; F: female; M: male; GCB: germinal center B-cell; ABC: activated B-cell; DEL: double expressor lymphoma; DHL: double hit lymphoma; THL: triple hit lymphoma; AJCC: the American Joint Committee on Cancer; LDH: lactate dehydrogenase; IPI: international prognostic index.

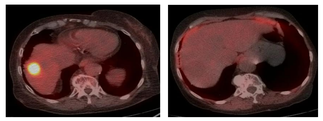
Table 2. Treatment and Response in Patients 1 - 7

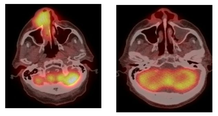
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Prior treatment, response	6 cycles R-CHOP, achieved CR (2018)[a]	Newly diagnosed DLBCL (patient undergoing hormonal therapy for stage 4 breast cancer)	None	1 cycle R-CHOP (2018)	None	None	None
Latest treatment	6 cycles R-CP + lenalidomide	3 cycles R_2-COP (achieved CR)[b]	6 cycles R_2-COP	5 cycles R_2-COP	6 cycles R_2-COP	6 cycles R_2-COP	6 cycles R_2-COP
Lenalidomide dose	25 mg × 21 days	25 mg × 21 days	25 mg × 21 days	10 mg × 14 days	25 mg × 14 days	25 mg × 14 days	20 mg × 21 days
Interim PET/CT scan, result	After 2 cycles, CMR	After 3 cycles, CMR	NA	After 2 cycles, CMR	After 3 cycles, CMR	After 4 cycles, CMR	After 3 cycles, CMR
Treatment duration, months	6	6	6	5	6	6	6
Best response	CR	CR	CR	CR	CR	CR	CR
Follow-up, months	24	44	4	24	20	48	3
Major treatment related-adverse event	No cytopenias	Grade 3 neutropenia	Grade 2 thrombocytopenia	Grade 4 neutropenia managed with growth factors	No cytopenias	Grade 3 neutropenia, one hospitalization for infection	Hepatitis B reactivation
Outcome	Alive, remains in CR	Alive, lymphoma remains in CR	Alive, remains in CR	Alive, remains in CR	Alive, remains in CR	Alive, remains in CR	Died from hepatitis B reactivation

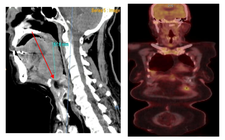
[a]Relapsed 1 year later. [b]Due to lenalidomide intolerance, treatment changed to cyclophosphamide, prednisone, and rituximab only for the last three cycles. Dosing: rituximab 375 mg/m^2, cyclophosphamide 750 mg/m^2, oral prednisone 100 mg daily for 5 days, and vincristine 1 mg. CMR: complete metabolic response; CR: complete response; DLBCL: diffuse large B-cell lymphoma; PET/CT: positron emission tomography/computed tomography; R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R-CP: rituximab, cyclophosphamide, and prednisone; R_2-COP: R-COP (rituximab, cyclophosphamide, vincristine, and prednisone) in combination with lenalidomide.

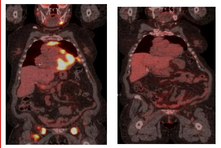
Interim PET CT scans after 2-4 cycles.

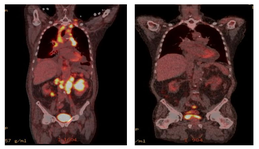

1. CMR

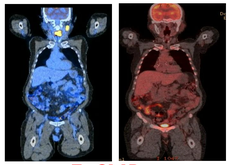

2. CMR


N.A.(After course 6)


4. CMR


5. CMR


6. CMR


7. CMR

CMR=complete metabolic response.

CONCLUSIONS

1. Lenalidomide plus an anthracycline-free regimen appears safe and effective and achieves durable remission in patients unfit for R-CHOP therapy.

2. An additional potential benefit of this regimen is the availability and potential reduction in cost in Third World countries.

The use of new therapies in this population of patients, such as bispecific antibodies alone ($180,000.00 X 8 courses) and/or in combination with targeted agents such as ibrutinib (ibrutinib cost $484.00 per capsule=$10,000.00 per 21 days course of treatment) can be economically prohibitive in Third World countries.

3. Larger studies are needed to evaluate a lenalidomide-anthracycline-free CI regimen's potential therapeutic and economic benefits.