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627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Retrospective Analysis of Clinical Outcomes of Utilizing R-CHOP Plus Zanubrutinib for High-Risk Diffuse Large B Cell Lymphoma Patients with Extranodal Involvement or MYC/BCL2 Double Expression

Wanbin Fu[1], *Jia Liu*[1], *Dan Xiao*[1], *Huanbin Zhao*[2], *Ting Wang*[1], *Jiong Hu*[3], *Jian Hou*[1], *Hua Zhong*[1], *Lan Xu*[1]

[1] Department of Hematology, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China
[2] Pharmaceutical Sciences Department, St. Jude Children's Research Hospital, Memphis, TN
[3] Shanghai Institute of Hematology, State Key Laboratory of Medical Genomics, National Research Center for Translational Medicine at Shanghai, Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China

Background: Diffuse large B-cell lymphoma (DLBCL) patients with extranodal involvement and double expression of MYC and BCL2 often have a poorer prognosis when treated with the standard first-line R-CHOP regimen. The 5-year progression-free survival (PFS) and overall survival (OS) rates are both below 40% for these high-risk DLBCL cases. In this study, we perform a retrospective analysis of the clinical outcomes and adverse events of the high-risk DLBCL patients with extranodal involvement and double expression, who were admitted to our center and used Bruton's tyrosine kinase inhibitor (BTKi) zanubrutinib on the basis of R-CHOP regimen.

Methods: We conducted a retrospective analysis of 26 DLBCL patients with extranodal involvement or MYC/BCL2 double expression who were admitted to our center and used R-CHOP regimen in combination with zanubrutinib between 1 st January 2021 and 30 th April 2023 (Figure A). Of these patients, 19 had extranodal involvement, and 7 were identified as double expression cases. The patients had a median age of 70 years, ranging from 34 to 87. Among them, 20 cases (77%) were aged over 60, and 8 cases (30%) were aged over 75. Moreover, 20 cases (76.9%) exhibited an Eastern Cooperative Oncology Group (ECOG) performance status score higher than 2 points. All the patients received an induction regimen consisting of zanubrutinib in combination with R-CHOP for a total of 4 cycles. After the fourth cycle, treatment efficacy was assessed using 18FDG-PET/CT scans. Patients achieving partial response (PR) or better continued with rituximab in combination with zanubrutinib for consolidation maintenance therapy, lasting for 1 year. For patients at risk of central nervous system involvement, oral administration of zanubrutinib continued for 2 years. During the treatment period, imaging evaluations were performed every 3 months to assess treatment response (Figure B).

Results: After the induction therapy, a mid-term PET/CT evaluation showed that all patients achieved PR or above, resulting in an overall response rate (ORR) of 100%. Among them, 19 patients (73.1%) achieved complete response (CR), while 7 patients (26.9%) achieved PR. During the consolidation and maintenance therapy, 7 patients who were initially in PR converted to CR. As of the latest follow-up, with a median follow-up duration of 11 months (ranging from 4.1 to 30.0 months), 2 patients (7.7%) were lost to follow-up, and 2 patients (7.7%) experienced disease progression. The median PFS and OS were not reached. The 2-year PFS was 69.7±13.4% (Figure C), and the 2-year OS was 77.4±12.2% (Figure D). Non-hematological adverse events included fatigue (38.5%), hypertension (15.38%), neurological symptoms (7.7%), and infections (100%). Among the infections, 3 cases (11.5%) were of >3-grade and led to treatment discontinuation. Additionally, one patient experienced immune encephalitis and went into a coma. Hematological adverse events included granulocytopenia (55%), anemia (26%), thrombocytopenia (42.3%), and bleeding (38.5%). Among them, >3-grade granulocytopenia occurred in 4.5% of the patients. Five patients who were on long-term anticoagulant therapy due to concurrent cardiovascular diseases experienced a reduction in zanubrutinib dosage during the follow-up period, resulting in an improvement in bleeding symptoms.

Conclusions: The combination of 4 cycles of R-CHOP regimen with zanubrutinib in the induction treatment of DLBCL patients with high-risk factors, such as extranodal involvement or MYC/BCL2 double expression, has shown promising clinical outcomes especially in older or unfit/frail patients. This approach allows for a reduction in the number of cytotoxic drug cycles, thereby improving the patients' tolerance to the treatment. Moreover, the efficacy of this regimen is superior to the traditional 6-8 cycles of R-CHOP induction therapy. Furthermore, the consolidation and maintenance therapy with rituximab in combination with zanubrutinib has demonstrated good safety and manageable adverse effects. This approach exhibits hope for further enhancing the prognosis of high-risk DLBCL patients.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: Zanubrutinib: diffuse large B cell lymphoma

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Clinical features of patients

Parameter	n	%	Parameter	n	%
Gender			Stage		
Male	15	57.7	I/II	8	30.8
Female	11	42.3	III/IV	18	69.2
Age			GA		
≤60	6	23.1	Fit	4	15.4
61-74	12	46.2	Unfit	5	19.2
≥75	8	30.8	Frail	17	65.4
PS			IPI		
<2	6	23.1	<2	11	42.3
≥2	20	76.9	≥2	15	57.7
Subtype			DEL		
GCB	6	23.1	No	19	73.1
non-GCB	20	76.9	Yes	7	26.9
No. of EN			EN site		
<2	13	68.4	Bone/BM	6	23.1
≥2	6	31.6	Breast	1	3.8
Molecular			Testicular	1	3.8
Subtype					
MCD	8	38.1	GI	5	19.2
TP53	5	23.8	CNS	4	15.4
BN2	3	14.3	Lung	1	3.8
EZB	2	9.5	Kidney/	8	30.1
			Adrenal gland		
N1	1	4.8			
ST2	2	9.5			

PS: performance statue; GA: geriatric assessment; IPI: international prognostic index; DEL: double expresser lymphoma; EN: extranodal; BM: bone marrow; GI: gastrointestinal CNS: central nervous system;

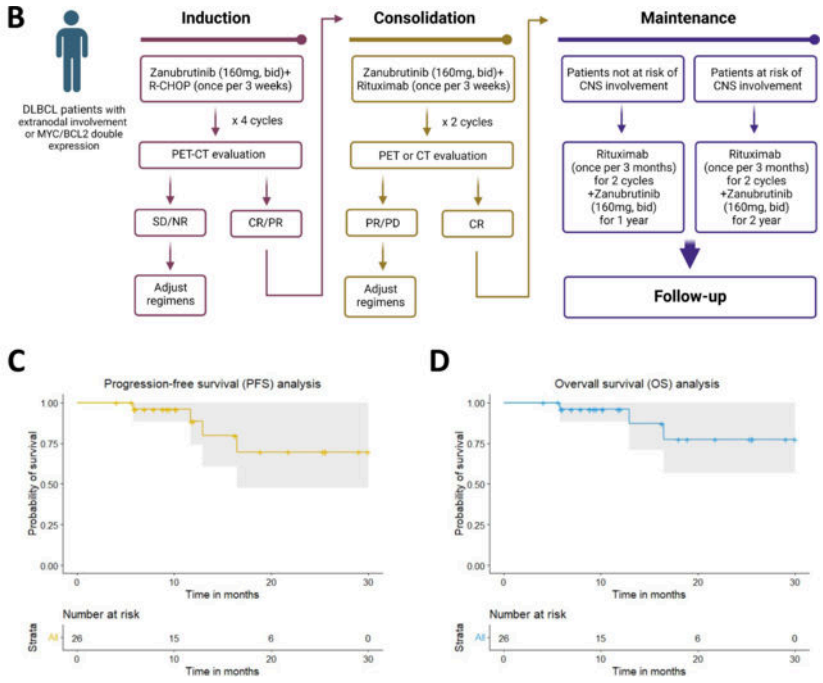

Figure 1

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