ELSEVIER

Blood 142 (2023) 5805–5806

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

605.MOLECULAR PHARMACOLOGY AND DRUG RESISTANCE: LYMPHOID NEOPLASMS

A Phase II Study of Chidamide Plus R-GDP Salvage Chemotherapy in Relapsed/Refractory Diffuse Large B-Cell Lymphoma Ineligible for Autologous Transplantation: Efficacy and Safety Analysis

Guangliang Chen[1], Kai Xue, MD[2], Qunling Zhang, MD PhD[3], Jia Jin[1], Yizhen Liu, MD PhD[4], Zuguang Xia[5], Fangfang Lyu[6], Xiaonan Hong[4], Xiaoqiu LI[5], Junning Cao[7]

[1] Fudan University, Shanghai, CHN
[2] Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, CHN
[3] fudan university, shanghai, China
[4] Fudan university, Shanghai, CHN
[5] fudan university, Shanghai, CHN
[6] fudan university, SHANGHAI, CHN
[7] Department of Lymphoma, Fudan University Shanghai Cancer Center, Shanghai, China

Background:
A significant subset of Diffuse large B-cell lymphoma (DLBCL) patients (30%-40%) face treatment failure, necessitating effective salvage chemotherapy. We conducted a phase II study evaluating the efficacy and safety of chidamide plus R-GDP (rituximab, gemcitabine, dexamethasone, cisplatin) in relapsed/refractory (r/r) DLBCL patients.
Methods:
This open-label, single-arm study included 27 patients with r/r DLBCL who were ineligible for autologous stem cell transplantation. Prior to the induction monotherapy phase, chidamide was administered orally at a dose of 30 mg twice a week for one week. The combination therapy phase consisted of oral chidamide at a dose of 20 mg twice a week for two weeks, with a one-week discontinuation period, along with intravenous administration of rituximab, gemcitabine, dexamethasone, and cisplatin on a 21-day cycle.
Results:
A total of 27 patients received at least one dose of Chidamide plus R-GDP and were evaluated for safety. The median follow-up period was 17.0 months (range: 3.5 to 55 months). Radiological response assessment was available for 24 patients, who constituted the efficacy population. Fourteen patients completed six cycles of chidamide plus R-GDP (per-protocol population), while 10 patients discontinued treatment at the data cutoff. The baseline characteristics of enrolled patients included a median age of 67 years, predominantly older than 65 years. Approximately half of the patients exhibited elevated lactate dehydrogenase levels. All patients had received prior therapy with R-CHOP or equivalent chemoimmunotherapy. The majority of cases were classified as stage III/IV and non-germinal center B-cell-like (non-GCB) type by immunohistochemistry. Refractory or relapsed DLBCL within 1 year since the last treatment was observed in 74.0% of patients.
Efficacy Outcomes:
The investigator-assessed best objective response rate (ORR) was 79.2% (95% CI: 75.1% to 83.3%), with a complete response (CR) rate of 45.8% (95% CI: 41.6% to 49.9%) and a partial response (PR) rate of 33.3% (95% CI: 29.3% to 37.4%). The median time to response was 1.2 months, and the median time to CR or CRu (unconfirmed complete response) was 3.9 months. The best disease control rate was 87.5%. Among the patients who completed six cycles of chidamide plus R-GDP, the best ORR was 100%, with 71.4% achieving CR and 28.6% PR. Kaplan-Meier plots reveal that the median investigator-assessed progression-free survival (PFS) for the efficacy population was 5.9 (95% CI, 3.1 to 12.4) months. The median overall survival was 48.3 (95% CI, 13.1 to not reach (NR)) months.
Safety Outcomes:
A total of 13 patients (48.1%) required treatment interruption, primarily due to adverse events (22.2%) and disease progression (18.5%). Among patients who completed six cycles of chidamide plus R-GDP, 57.1% required a chidamide dose reduction. The most frequent treatment-emergent adverse event was anemia, occurring in all patients. Thrombocytopenia was the most common grade ≥3 adverse event leading to treatment interruption or dose reduction, affecting 48.1% of patients.

Non-hematologic events included hypocalcemia (59.3%), hyponatremia (55.6%), and hypokalemia (44.4%). Three patients experienced grade 3 pneumonitis, and one patient had grade 3 skin rash.

Conclusion:

Chidamide plus R-GDP salvage chemotherapy demonstrated promising efficacy (ORR: 79.2%; CR rate: 45.8%) in r/r DLBCL patients. Adverse events were manageable but necessitated monitoring. Larger trials are needed to validate these findings and establish chidamide plus R-GDP as a potential treatment option for this challenging population.

Keywords: relapsed/refractory DLBCL, salvage chemotherapy, chidamide, R-GDP, efficacy, safety

Disclosures No relevant conflicts of interest to declare.

Table 1. Baseline patient and disease characteristics.

	Patients in safety population (n=27)
Age, years	
Median (Range)	67 (51-74)
Age ≥ 65 years, n (%)	21 (77.8)
Sex	
Male, n (%)	13 (48.1)
Female, n (%)	14 (51.8)
ECOG performance-status score	
1, n (%)	25 (92.5)
≥ 2, n (%)	2 (7.4)
Stage III/IV, n (%)	23 (85.2)
Increased lactate dehydrogenase, n (%)	12 (44.4)
Cell of origin (by immunohistochemistry), n (%)	
GCB	10 (37.0)
non-GCB	15 (55.6)
Unknown	2 (7.4)
Patients with transformed lymphoma, n (%)	
Follicular lymphoma	2 (7.4)
Marginal zone lymphoma	1 (3.7)
Number of previous treatments, n (%)	
1	25 (92.6)
2	2 (7.4)
First-line therapy, n (%)	
CHOP	1 (3.7)
R-CHOP	19 (70.4)
R-CHOP+X	7 (25.9)
Type of disease at inclusion, n (%)	
Relapse*	8 (29.6)
Refractory**	19 (70.4)
Time since DLBCL diagnosis, months (95%CI)	14 (11.0-18.0)
Less than 1 year since last treatment, n (%)	20 (74.1)

ECOG, Eastern Cooperative Oncology Group; GCB: germinal center B cell. DLBCL, Diffuse large B-cell lymphoma. R-CHOP, Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and oral Prednisolone. CI, confidence interval. *Relapse refers to lymphoma, which recurs or develops after a period of complete remission. **Refractory was defined as patients with stable or progressive lymphoma after first-line treatment.

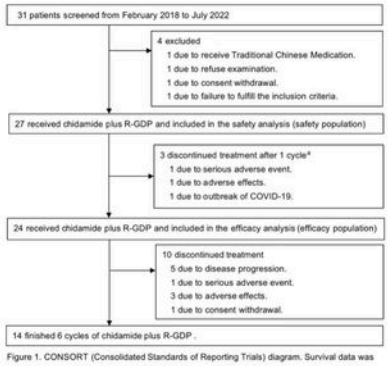

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram. Survival data was collected up until the October 20, 2022 data cut-off. R-GDP, rituximab, gemcitabine, dexamethasone, cisplatin. * Radiological post-baseline response assessment not performed/data unavailable.

Table 2. Investigator assessed best overall response.

	Efficacy population (n=24)
Best objective response, n (%)	
Complete response	11 (45.8)
confirmed CR with FDG-PET*	9 (37.5)
Partial response	8 (33.3)
Stable disease	2 (8.3)
Progressive disease	3 (12.5)
Objective response, n (%) (all patients)	19 (79.2)
Disease control	21 (87.5)

Data are number of patients (%) with cut off on Oct 20, 2022.
DLBCL: diffuse large B-cell lymphoma; PP, per-protocol.
* FDG-PET, 18-Fluorodeoxyglucose positron emission tomography.
CR: Complete response;
Objective response: complete + partial responses;
Disease control rate: complete + partial responses + stable disease;

Figure 2, Survival analysis of patients in the efficacy population (n=24). Analyzed by using Kaplan-Meier methodology for progression-free survival (PFS) (A) and overall survival (OS) (B); censored patients are indicated. NR, not reach.

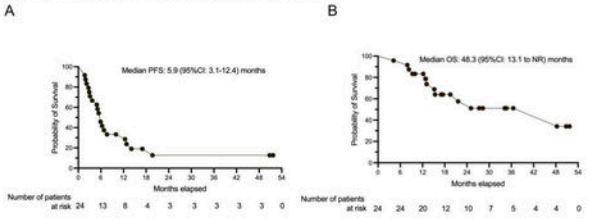

Figure 1

https://doi.org/10.1182/blood-2023-174307