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POSTER ABSTRACTS

614.ACUTE LYMPHOBLASTIC LEUKEMIAS: THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Venetoclax, Cladribine and Cytarabine for the Treatment of Relapse/Refractory Acute Lymphoblastic Leukemia: Interim Analysis of a Phase 2 Trial

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Venetoclax, cladribine and cytarabine for the treatment of relapse/refractory acute lymphoblastic leukemia: interim analysis of a phase 2 trial

Background: Philadelphia chromosome-negative acute B lymphoblastic leukemia (Ph- B-ALL) accounts for approximately 60-70% of adult B-ALL. Patients with relapse/refractory (R/R) Ph- B-ALL was reported to have a poor prognosis. Immunotherapies such as blinatumomab, CAR T-cell therapy achieved high response rate for Ph- B-ALL. However, salvage chemotherapies are also worth of investigation because many patients can't afford immunotherapies. We found that venetoclax, cladribine and low-dose cytarabine had synergistic cell toxicity against B-ALL cell line RS4;11 in our previously in vitro studies. Based on these findings, we designed a multicenter, phase 2 study utilizing the venetoclax, cladribine and cytarabine (CAV) regimen for the treatment of R/R B-ALL (NCT05657652).

Methods: The CAV regimen consisted of cladribine 5 mg/m ^{2}/day from day 1 to day 3 or day 5, cytarabine 20mg/m ^{2}, q12h, for 7-10 days and venetoclax 100mg d1, 200 mg d2, 400 mg/day from day 3 to day 28. Bone aspiration evaluation was performed at 14-28 days after the completion of CAV regimen. Treatment responses were evaluated according to the NCCN guidelines. The threshold of MRD negativity was defined as less than 0.01% as detected by multiparameter flow cytometry.

Results: Since February 2021, a total of 16 patients with R/R Ph- B-ALL were enrolled in this study. Baseline characteristics of these patients were summarized in Table 1. The median age was 36 years (range, 13-66 years), and 12/16 (75%) patients were male. Among them, 12 patients (75%) had relapsed Ph- B-ALL and 4 patients (25%) had refractory Ph- B-ALL. One patient had concurrent active central nervous system leukemia. One patient had a complex karyotype, and two patients had TP53 mutations. Treatment responses were shown in Table 2. 12/16 (75%) patients responded to CAV regimen after one cycle of CAV regimen, with 3/16 (18.75%) with complete remission (CR), 8/16 (50%) with CRi, and 1/16 (6.25%) with morphology leukemia-free state (MLFS). Among patients who achieved treatment response, 9/12 (75%) patients attained MRD negativity. During the treatment with the CAV regimen, one patient (1/16, 6.3%) developed grade 4 tumor lysis syndrome. 4/16 (25%) patients suffered grade 3 to 4 infections. Grade 1 to 2 gastrointestinal reactions and liver dysfunction were observed in 8/16 (50%) and 5/16 (31.3%) patients, respectively. The 60-day mortality rate was 6.3%. Two patients who relapsed after CAV treatment re-achieved remission after CART therapy. Nine patients received allo-HSCT after CAV regimen. With a median follow-up of 11 months (range, 0.3-28 months), the estimated 1-year overall survival rate was 76.2% and 1-year event-free survival rate was 38.4%. The survival swimming plot was shown in Figure 1. The median OS was not reached and the median EFS was 13 months. The cumulative relapse rate was 31.3% (5/16). At the last follow-up, two patients died of relapse, one patient died of cerebral hemorrhage and one patient died of sepsis.

Conclusion: In summary, our results demonstrated that CAV regimen showed encouraging efficacy and safety in treating R/R Ph- B-ALL patients.

Disclosures No relevant conflicts of interest to declare.

Table 1 Baseline characteristics of the patients

Baseline Characteristics	
Age, years	36 (13-66)
Gender	
Male	12 (75%)
Female	4 (25%)
WBC count, 10^9/L	7.9 (1.55-171.95)
Percentage of blasts before CAV, %	60 (3-94)
Previous therapy	
1 line	8 (50%)
2 lines	5 (31.3%)
≥ 3 lines	3 (18.8%)
Cytogenetics at diagnosis	
Complex karyotype	1 (6.3%)
t(1;4)	1 (6.3%)
14q+	1 (6.3%)
Mutations at diagnosis	
TP53	2 (12.5%)
IKZF1	2 (12.5%)
FLT3	1 (6.3%)
SH2B3	1 (6.3%)
Relapsed	12 (75%)
Intramedullary relapse	11 (91.6%)
Extramedullary relapse	1 (8.3%)
Refractory	4 (25%)

Table 2 Treatment responses of the patients

Treatment responses	
ORR, No. (%)	12 (75%)
CR, No. (%)	3 (18.8%)
CRi, No. (%)	8 (50.0%)
MLFS, No. (%)	1 (6.3%)
Aplastic marrow, No. (%)	0
PR, No. (%)	4 (25%)
MRD negative rate by MFC, No. (%)	9 (75%)
Proceeded to allo-HSCT, No. (%)	9 (56.3%)
Overall survival, median, mo	Not reached
Event-free survival, median, mo	13
1-year overall survival rate	76.2%
1-year event-free survival rate	38.4%

Figure 1 Swimming plot of the patients

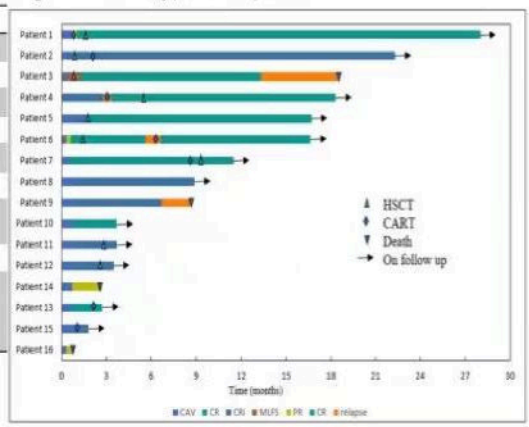

Figure 1

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