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ORAL ABSTRACTS

615.ACUTE MYELOID LEUKEMIAS: COMMERCIALLY AVAILABLE THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Comparing the Efficacy and Safety of Venetoclax Combined with Decitabine Versus Conventional Chemotherapy As Induction Therapy for Young Adults with Newly Diagnosed Acute Myeloid Leukemia - Interim Analysis of a Multicenter, Randomized, Phase 2b Trial

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Introduction: Venetoclax in combination with hypomethylating agents (HMAs) is a first-line induction regimen recommended by NCCN guidelines for older or unfit AML patients. In a phase 2 study (NCT04752527) from our group, venetoclax plus decitabine (VEN-DAC) resulted in a 93% of response rate in young adult patients with newly diagnosed (ND) ELN adverse-risk AML. Currently, there is a lack of data on the VEN-DAC regimen in ND young adults with favorable or intermediate risk AML who are fit for intensive chemotherapy. There are also no studies directly comparing the VEN-DAC regimen with intensive chemotherapy in patients with ND AML. Here, we report the results of an interim analysis of a multicenter, randomized, phase 2b trial (NCT05177731) , which explored the efficacy and safety of VEN-DAC versus intensive chemotherapy (idarubicin and cytarabine) in ND AML patients.
Methods: Adult patients with newly diagnosed AML aged between 18 and 59 years were enrolled. The diagnosis was made according to the WHO 2016 criteria. Risk stratification was performed according to the 2017 ELN recommendations. Eligible patients were randomized in a 1:1 ratio to the VEN-DAC group (decitabine 20mg/m ^{2} on days 1-5 and venetoclax at an escalated dose of 100mg, 200mg and 400mg by day 28) or the IA-12 group (idarubicin 12mg/m ^{2} on days 1-3 and cytarabine 100mg/m ^{2} on days 1-7). Patients who did not respond to the treatment were allowed to receive another cycle of the original induction regimen. Intermediate-dose cytarabine (2g/m ^{2}, q12h, days 1-3) were applied as consolidation therapy. The primary endpoint was the composite complete remission (CRc, including complete remission, CR and complete remission with incomplete hematologic recovery, CRi). The secondary endpoints included measurable residual disease (MRD) negative remission (defined as $<1\times10^{-3}$ by flow cytometry), event-free survival (EFS) , overall survival (OS) and adverse events.
Results: Since March, 2022, a total of 163 patients with AML were screened and 116 patients were randomized. Sixty patients received the VEN-DAC regimen and 55 patients received the IA-12 regimen. There were no differences in baseline characteristics between the two groups of patients (Table 1). Bythe cut-off date of July 11, 2023, a total of 102 patients have been evaluated, 55 in the VEN-DAC group and 47 in the IA-12 group. The overall CRc rate in the VEN-DAC group was 85.5%, which was comparable to that of the IA-12 group (78.7%, P=0.37). The MRD-negative CR rate in the VEN-DAC group was 67.3%, which was much higher than that in the IA-12 group (53.2%) (P=0.147). According to univariate analysis, efficacy of the VEN-DAC regimen did not differ from that of the IA-12 regimen with respect to sex, age, initial bone marrow blast count, genetic risk category, and major molecular markers (Figure 1A). Notably, the CRc rate and MRD-negative CR rate were significantly higher in the VEN-DAC group than in the IA-12 group for intermediate-risk and adverse-risk patients, especially those with adverse risk (P=0.031 for CRc, P=0.029 for MRD-negative CR) (Figure 1A). At median follow-ups of 7.8 months (range, 0.9-16.6), the EFS and OS were not reached in both groups. The median time for platelets to recovery to 20×10^{9}/L or above in the VEN-DAC group was 12 days after induction in the VEN-DAC group, which was shorter than that in the IA-12 group (21 days) (P<0.01). In addition, patients in the VEN-DAC group required fewer platelet (5 U vs 7 U, P<0.01) and red blood cell infusions (3 U vs 5 U, P=0.023) during induction as compared with that in the IA-12 group. In addition, the incidence of grade 3 or higher febrile neutropenia (41.8% vs. 83.0%), infection (27.3% vs. 72.3%) and sepsis (5.5% vs. 31.9%) were all significantly lower in the VEN-DAC group than in the IA-12 group (P<0.01) (Figure 1B).

Conclusion: In newly diagnosed young AML patients, venetoclax in combination with decitabine as an induction regimen had comparable efficacy and a higher safety profile compared to IA-12 regimen. In particular, patients with adverse-risk AML showed higher and deeper remission rate in the venetoclax plus decitabine group as compared with the IA-12 group.

Disclosures No relevant conflicts of interest to declare.

Table 1. Baseline characteristics of all the enrolled patients

Baseline characteristics	VEN+DAC (N=60)	IA-12 (N=56)	P
Sex, n (%)			0.10
Male	31 (51.7)	63 (64.3)	
Female	29 (48.3)	20 (35.7)	
Age, median (range)	44 (21-59)	39 (20-59)	0.24
Bone marrow blast count, median (range),%	55 (14-97)	63 (12-96)	0.78
Genetic risk according to ELN-2017, n (%)			0.12
Favorable	28 (53.8)	28 (60.9)	
Intermediate	14 (26.9)	5 (10.9)	
Adverse	10 (19.2)	13 (28.3)	
Fusion genes / somatic mutations			
RUNX1::RUNX1T1	8 (13.3)	10 (17.9)	0.50
CBFB::MYH11	4 (6.7)	9 (16.1)	0.11
FLT3-ITD	11 (18.3)	6 (10.7)	0.25
NPM1	11 (18.3)	4 (7.1)	0.073
CEBPA^{bZIP}	14 (23.3)	11 (19.6)	0.63

Figure 1. Comparative analysis for efficacy (CRc and MRD-negative) (A) and safety (B) of VEN-DAC versus IA-12 in induction therapy cycle 1

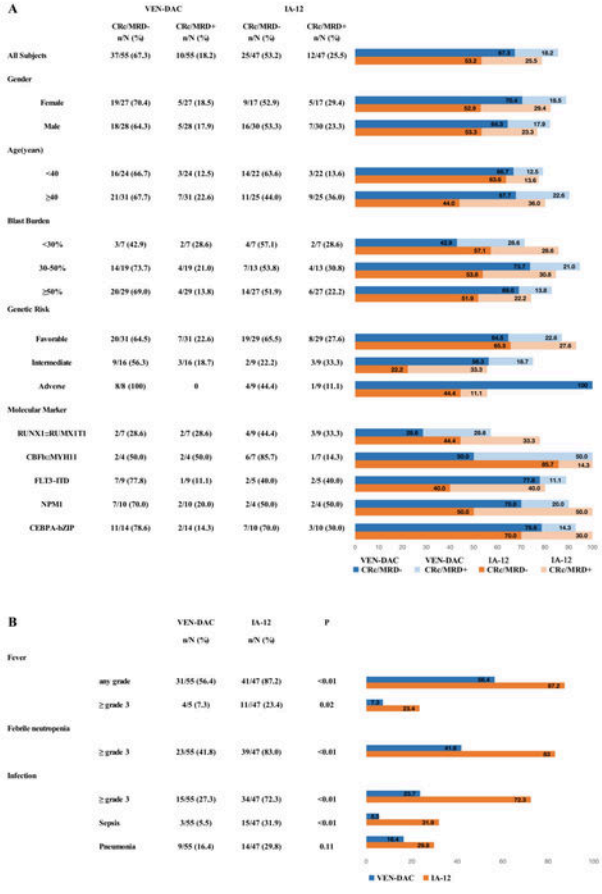

Figure 1

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