Abstract: PB1857

Title: VENETOCLAX, AZACITIDINE, COMBINED WITH LOW-DOSE CYTARABINE IN OLDERLY OR UNFIT PATIENTS WITH NEWLY DIAGNOSED ACUTE MYELOID LEUKEMIA

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Background:

Older or unfit patients with acute myeloid leukemia (AML) have a dismal prognosis. The combination of venetoclax with azacitidine had promising efficacy, and well tolerated in elderly patients with AML, but the minimal residual disease (MRD) negative rate is only 30-40%.In most cases measurable residual disease (MRD) positivity predicts hematologic relapse potentially allowing early therapeutic intervention.

Aims:

To explore the efficacy and safety of Ven+AZA+LDAC induction therapy for older or unfit adult AML.

Methods:

This is a prospective, one-arm, multicenter, open clinical trial, Adults age ≥18 years with newly diagnosed AML ineligible for intensive chemotherapy were enrolled.Patients received induction treatment with venetoclax 100mg d1 200mg d2 400mg d3-28, azacytidine 75mg/m^2 d1-7, cytarabine10mg/m^2 q12h d1-7. The primary observation was the remission rate(CR/CRi) and the negative rate of MRD. Secondary end points included total effective rate (ORR), safety and tolerability, including dose limiting toxicity (DLT) and adverse events (AE).

Results:

the baseline characteristics of 20 older or unfit patients who can evaluate the efficacy are shown in Table 1.

After the first course of Ven+AZA+LDAC treatment, 12 patients (60%) reached CR with negative MRD, 5 patients (25%) reached CR with positive MRD, 2 patients (10%) had partial remission (PR), 1 patient (5%) had no remission (NR), and the ORR was 95%. Subgroup analysis showed that of 11 elderly patients, 8 (72.7%) had CR with MRD negative, 2 (18.2%) had CR with MRD positive, and 1 (9.1%) had partial remission (PR); Of the 9 patients initially diagnosed with unfit, 7 (77.8%) reached CR, of which 4 (57.1%) were negative for MRD, 1 (11.1%) had partial remission (PR), and 1 (11.1%) had no remission (NR).

Safety: All the 11 elderly patients had febrile neutropenia, which controlled after therapy, without severe infection and bleeding complications. 9 patients with unfit had severe complications such as severe infection, respiratory failure, or intracranial hemorrhage before treatment, but no treatment-related deaths occurred during the induction period. Related adverse reaction are shown in Figure 1.

Summary/Conclusion:

In conclusion, in newly diagnosed patients who were ineligible for intensive chemotherapy, the incidence of remission was higher among patients who received Ven+AZA+LDAC, and some patients can quickly obtain negative MRD. Infection, chemotherapy-related mortality, and the tolerability were acceptable. However, it is necessary to further expand the sample size and extend the follow-up time to assess the long-term survival rate.

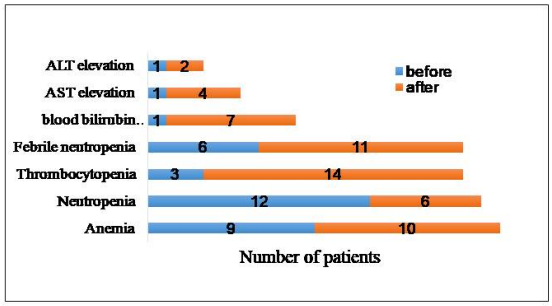
Table 1. Patient Clinical Characteristics

Characteristic	N=20
Median (range), years	57.4 (32-73)
Older, n(%)	11(55%)
Unfit, n(%)	9 (45%)
Male, n (%)	13 (65%)
Bone marrow blast count, n(%)	
20-30%	5 (25%)
≥30 - <50%	4 (20%)
≥50%	11 (55%)
Baseline neutropenia, n(%)	
Grade 3	2 (10%)
Grade 4	9 (45%)
FAB classification, n(%)	
AML-M1	3 (15%)
AML-M2	7 (35%)
AML-M4	5 (25%)
AML-M5	3 (15%)
Cytogenetic risk category, n(%)	
Favorable	4 (20%)
Intermediate	8 (40%)
Poor/Adverse	8 (40%)
Somatic mutations	
FLT3	8 (40%)
NPM1	3 (15%)
IDH1	3 (15%)
DNMT3A	4 (20%)
TP53	1 (5%)
Transfusion dependent at baseline, n(%)	
Red blood cells	8 (40%)
Platelets	7 (35%)

Table 2. Efficacy results

	Older AML (n=11)	Unfit AML (n=9)
ORR	11/11 (100%)	8/9 (88.9%)
mCRc	10 (90.9%)	7 (77.8%)
CR	7 (63.6%)	6 (66.7%)
CRi	3(27.3%)	1 (11.1%)
PR	1/11(9.1%)	1 (11.1%)
NR	0	1/9(11.1%)

Figure 1. Related adverse reaction



Keywords: Aging, Venetoclax, AML