Abstract: P544

Title: VENETOCLAX PLUS AZACITIDINE, CYTARABINE, ACLARUBICIN AND G-CSF (VA-CAG REGIMEN) FOR NEWLY DIAGNOSED PATIENTS WITH ACUTE MYELOID LEUKEMIA: UPDATE OF A PROSPECTIVE, MULTICENTER, PHASE 2 CLINICAL TRIAL

Abstract Type: Poster Presentation

Topic: Acute myeloid leukemia - Clinical

Background:

Although the combination of anthracycline and cytarabine has achieved a remission rate of about 70% in newly diagnosed acute myeloid leukemia (AML) patients, the low complete response rate in adverse-risk patients, strong adverse reactions, and long duration of myelosuppression limited the clinical benefit. Venetoclax, in combination with hypomethylating agents or low-dose cytarabine, is approved for newly diagnosed AML patients who are over 75 years of age or not eligible for intensive chemotherapy, while the efficacy of venetoclax-based regimens in young fit AML patients still needs to be further explored.

Aims:

We conducted a prospective, multicenter, single-arm phase 2 clinical trial and update our data to explore whether the VA-CAG regimen (venetoclax plus azacitidine in combination with low-intensity CAG regimen) could have a better complete remission with an acceptable safety profile.

Methods:

This study was approved for ethical review and registered with ClinicalTrials.gov (NCT05662956). Patients who were newly diagnosed with AML aged from 18 to 65 years without active infection, bleeding and severe cardiopulmonary insufficiency were enrolled. Participants received induction as azacitidine 75 mg/m2 subcutaneously once daily on days 1-7, cytarabine 10mg/m2 subcutaneously q12h on days 1-7, aclacinomycin 12 mg/m2 on days 1,3,5,7, granulocyte colony-stimulating factor 5ug/kg on days 1-7, and venetoclax orally once daily (100 mg d1, 200 mg d2, 400 mg d3-21). Venetoclax dose was adjusted based on concomitant CYP3A inhibitors. The efficacy were evaluated by bone marrow morphology and flow cytometry on day 28 cycle 1. The primary endpoints were the complete remission rate and safety.

Results:

A total of **s**ixty-seven patients from twelve sites were enrolled between January 1, 2023, and January 25, 2024. The median age was 51 years (range, 18-63). Thirty patients (44.8%) had adverse risk, 19 patients (28.4%) had intermediate risk, 14 patients (20.9%) had favorable risk and 4 patients (5.9%) had indeterminate risk. The overall remission response rate after one cycle was 98.5% (66/67), including 94.0% (63/67) complete remission and 4.5% (3/67) partial remission. 52(82.5%) out of 63 patients who reached complete remission were MRD negative by flow cytometry. Fifty-three patients (79.1%) used azole drugs to prevent or treat fungal infection. The most common grade 4 adverse events included neutropenia (97.0%), thrombocytopenia (85.1%) and infection (14.9%). The Duration of ≧ grade 4 neutropenia and ≧ grade 4 thrombocytopenia were 13.5 days (range, 0-33) and 7 days (range, 0-23), respectively. The median red blood cell and platelet transfusions were 6u (range, 0-19.5) and 30u (range, 0-170), respectively. Eleven patients (10.4%) had a breakthrough invasive fungal infection and 3 patients (4.5%) experienced sepsis, but with good management. No treatment-related death occurred. After a median follow-up of 6 months, 14 patients underwent hematopoietic stem cell transplantation, the overall survival rate was 92.5%.

Summary/Conclusion:

VA-CAG regimen achieved high rates of complete remission and MRD negative in young adult fit patients with

newly diagnosed AML. This combined regimen has an acceptable safety profile, with low incidence of infection and transfusion dependence.

Figure 1. Response assessment and adverse events.

Efficacy and safety assessment	N(%) / Median (range)
Overall response rate (ORR)	66 (98.5)
Complete remission (CR)	63 (94.0)
Partial remission (PR)	3 (4.5)
No response (NR)	1 (1.5)
Measurable residual disease-negative in patients with CR	52 (82.5)
Duration of ≧ grade 4 neutropenia, days	13.5 (0-33)
Duration of ≧ grade 4 thrombocytopenia, days	7.0 (0-23)
Red cell transfusion, n (unit)	6 (0-19.5)
Platelet transfusion, n (unit)	30 (0-170)
≧ Grade 4 neutropenia	365(97.0)
≧ Grade 4 thrombocytopenia	57 (85.1)
Pneumonia	7 (10.4)
Sepsis	3 (4.5)
Tumor lysis syndrome	0 (0)
Seveve bleeding events	0 (0)
treatment-related death mortality	0 (0)

Keywords: AML, Multicenter, Venetoclax