Abstract: PB2640

Title: DOES VENETOCLAX IMPROVE OUTCOMES IN HIGH-RISK MYELODYSPLASTIC SYNDROME? A RETROSPECTIVE MULTICENTER STUDY COMPARING AZACITIDINE-VENETOCLAX VS. AZACITIDINE MONOTHERAPY IN MEXICO

Abstract Type: Publication Only

Topic: Myelodysplastic syndromes - Clinical

Background:

High-risk myelodysplastic syndromes (HR-MDS) identified by the Revised International Prognostic Scoring System (IPSS-R) with a score >3.5 points are associated with an increased risk of progressing to acute myeloid leukemia (AML), with a median overall survival (OS) of 18.6 months (95% CI; 15.3-21.9). Standard treatment for HR-MDS patients ineligible for allogeneic hematopoietic stem-cell transplantation (HSCT) involves hypomethylating agents, with overall response rates (ORR) of 30% in phase 3 studies published in 2009. Recent phase 1b studies indicate that adding venetoclax, may enhance response rates in clinical settings, showing an ORR of 80% with a toxicity profile similar to that of hypomethylating agents alone. The treatment of patients with HR-MDS is an unresolved necessity.

Aims:

Determining whether adding venetoclax to the hypomethylating agent improves overall survival in patients with HR-MDS.

Methods:

We conducted a retrospective multicenter study analyzing outcomes of HR-MDS patients treated between 2011 and 2023 across four institutions in Mexico. Definitions for complete response (CR), complete response with incomplete cell count recovery (CRi), partial response (PR), and hematological improvement (HI) were based on IWG-2023 criteria. ORR included CR, CRi, PR, and HI. Bivariate analysis was conducted to detect differences in baseline characteristics, adverse events (AEs), and response rates between treatment groups. Kaplan-Meier curves were generated for OS analysis.

Results:

We analyzed 51 HR-MDS patients, with 35 (68.6%) being male and a median age of 67 years (IQR; 61-74). ECOG scores were <2 points for 43 patients (84%). According to the 2022 WHO classification, 14 patients (31.5%) had low blast burden, 15 (29.5%) had high blast burden type 1, and 18 (35%) had type 2. 27 patients (52.9%) had more than 5% blasts. NGS myeloid mutation panel was performed in 14 (27.4%) patients, revealing biallelic-TP53 mutations in two.

We identified 33 (65%) patients treated with azacitidine-venetoclax and 18 (35%) with azacitidine, with 10 patients (19.6%) undergoing HSCT. No baseline characteristic differences were noted between groups.

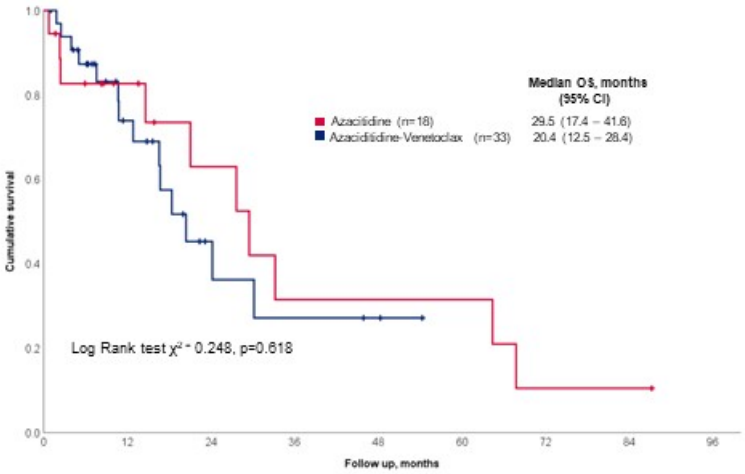
ORR was achieved in 38 (74.5%), with 10 (19.5%) responding to the first cycle and 11 (21.5%) to subsequent cycles; 12 (23.5%) achieved CR and 5 (10%) achieved CRi. Thirteen (34%) responders relapsed. Mortality in the first 8 weeks did not differ between groups. Adverse events were observed in 36 (88%) patients. Hematologic toxicities did not differ between azacitidine-venetoclax and azacitidine groups: anemia (22(82%) vs. 10(67%), thrombocytopenia 23(85%) vs. 11 (73%), neutropenia 25(93%) vs. 12(80%), and febrile neutropenia 14 (52%) vs. 9 (60%).

Median OS was 24.2 months (95% CI 12.3-34.1). No statistically significant differences in OS were found between azacitidine-venetoclax and azacitidine-only groups (median 20.4 vs. 29.5 months; p=0.618).

Summary/Conclusion:

The management of HR-MDS in patients ineligible for HSCT remains a pressing challenge. Given the promising role of venetoclax in AML, its potential in HR-MDS warranted investigation in this study. However, our findings revealed no significant differences in overall responses, complete responses, hematologic improvements, or overall survival. While adverse events were more common in the venetoclax group, this disparity did not reach statistical significance, likely due to the limited sample size. Nonetheless, these insights have informed our current practice of treating patients exclusively with hypomethylating agents as monotherapy in our centers.

Figure 1. Overall Survival by Treatment Group



Keywords: Hypomethylating agents, Myelodysplastic syndrome, Myelodysplasia, Myeloid malignancies