Abstract: P567

Title: VENETOCLAX-AZACITIDINE VERSUS AZACITIDINE FOR THE TREATMENT OF ACUTE MYELOID LEUKEMIA (AML) IN FIRST RELAPSE OR PRIMARY REFRACTORY TO INTENSIVE CHEMOTHERAPY. AN IPC-DATAML-MSKCC STUDY

Abstract Type: Poster Presentation

Topic: Acute myeloid leukemia - Clinical

Background:

The use of Azacitidine (AZA) as salvage therapy for AML patients failing intensive chemotherapy (IC) is associated with an overall response rate of approximately 20-30% and an overall survival of 7-9 months. Although commonly used, there is limited data regarding the addition of Venetoclax (VEN) to AZA (VEN-AZA). While it has been shown that VEN-AZA is superior to AZA alone in prior untreated AML patients this is not clear for patients with relapsed/refractory AML.

Aims:

The aim of this study is to compare the efficacy of VEN-AZA to AZA salvage therapy in AML fit patients failing IC.

Methods:

We extracted data from from 2 French registries (Institut Paoli Calmettes [Marseille] n= 168, DATAML [Toulouse-Bordeaux] n=166), and one from US (MSKCC, [New York] n=10), comprising patients treated with VEN-AZA in first relapse or primary refractory to one or two cycles of IC, who were treated with VEN-AZA between September 2017 and 2023. Patients previously treated with VEN and those with molecular relapse AML were excluded from the analysis. This cohort was compared to patients from the three registries treated with AZA monotherapy between 2010 and 2022.

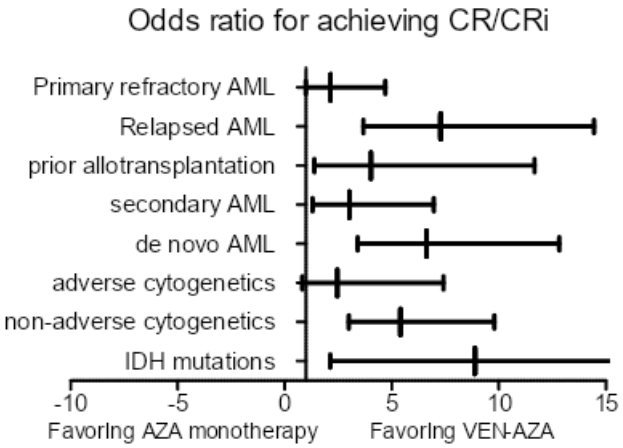
Results:

We compared 134 patients treated with VEN-AZA with 210 patients treated with AZA. There were no significant differences in terms of median, 67 *vs* 65 years, disease stage (relapsed [67.2% vs 64.3%]*vs* primary refractory [32.8% vs 35.7%]), prior allogeneic stem cell transplantation (ASCT, 23.1 *vs* 28.6%), and ECOG performance status = 0-1 (79.8% *vs* 76.7%), between the two groups. The median CR1 duration was 12 months (interquartile range ([IQR], 8-22) in the VEN-AZA group vs 10 months, (IQR, 6-18); p=.153). Cytogenetic risk was favorable, intermediate, and adverse in 3%, 68%, and 29% in the VEN-AZA group and 0.5%, 67%, 32.5% in the AZA group, with no significant differences. *FLT3*-ITD, *NPM1*, *IDH1/2*, and *TP53* mutations were found in 6%, 18%, 28%, and 24% in the VEN-AZA group vs 16%, 15%, 18%, and 25% in the AZA group (p= .008, .999, .128, and .168, respectively). Response evaluation was available for 304 patients. The complete response rate (CR) + CR with incomplete hematological recovery (CRi) with VEN-AZA *vs* AZA treatment was 54.9% *vs* 22.5% (p<.001) including a CR rate of 41.9% vs 16.7% (p<.001) and a CRi rate of 12.9% vs 5.7% (p=.04). The composite response rate including partial response and morphological leukemia-free state was 70% vs 33% (p<.001). Almost all the subgroups of patients achieved a better CR/CRi with VEN-AZA than AZA (**Figure 1**). Day-30 and day-100 mortality rates were 6.3% and 28.8% with VEN-AZA *vs* 11.7% and 40.9% with AZA alone (p=.117 and .210, respectively). ASCT following salvage treatment was 23% vs 12% (p=.007). Most of the ASCT were perfomed in CR/CRi with VEN-AZA group (80.6%) vs 45.8% in the AZA group (p=.01). Median follow-up was 15 months in the VEN-AZA group (IQR, 9-22), and 68 months (IQR, 24-88) in the AZA group. Median OS from day-1 of salvage treatment was 10 months (IQR, 4-23) *vs* 7 months (IQR, 3-16); p= .01) in the VEN-AZA vs AZA group, respectively. Median OS of patients who undergone ASCT after salvage VEN-AZA was not reached compared to 17 months for AZA patients (p=.29). Median OS in the non-transplanted patients were 8 vs 6 months in the VEN-AZA vs AZA groups, respectively. In multivariate analysis considering age, salvage

treatment, cytogenetics, major mutations (*FLT3*-ITD, *NPM1*, *IDH*1/2 and TP53), and prior ASCT, prognostic factors influencing survival were VEN-AZA salvage treatment and adverse cytogenetics with a hazard ratio of 0.41 (95% CI, 0.22-0.78) and 3.12 (95% CI, 1.61-6.03), respectively. **Summary/Conclusion:**

VEN-AZA salvage treatment is associated with higher CR/CRi rates and ASCT realization, resulting in a longer OS compared to AZA monotherapy. This treatment could constitute a new therapeutic standard for AML failing IC as part of a "bridge to transplant" strategy.

Figure



Keywords: Acute myeloid leukemia, Acute monoblastic leukemia, AML