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PB2005 AZACITIDINE IN COMBINATION WITH 14-DAY VENETOCLAX VERSUS AZACITIDINE MONOTHERAPY FOR MYELODYSPLASTIC SYNDROME WITH INCREASED BLASTS-2 IN CLINICAL PRACTICE SETTING

Topic: 10. Myelodysplastic syndromes - Clinical

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Background:

Azacitidine (AZA) is the standard-of-care for myelodysplastic syndromes with increased blasts-2 (MDS-IB2), however, due to the limited efficacy there is an unmet need for more effective therapies. Recently, promising phase 1 data of Azacitidine and Venetoclax (AZA+VEN) have been published and the phase 3 Verona trial is ongoing. Herein, we compared our institutional experience of AZA+VEN doublet with AZA monotherapy for the treatment of MDS-IB2.

Aims:

The aim of our study was to compare the efficacy and toxicity of AZA+VEN with AZA monotherapy for MDS-IB2 treatment.

Methods:

We conducted an observational, retrospective study. The patients were older than 18 years of age, had newly diagnosed MDS-IB2, and were treated with either AZA+VEN or AZA monotherapy. All patients provided informed consent for treatment and data collection. The AZA+VEN regimen consisted of Venetoclax 400mg/d on days 1-14 with Azacitidine 75mg/m2 on days 1-7. AZA patients received Azacitidine 75mg/m2 on days 1-7. The treatment cycles were administered every 28 days or with longer intervals depending on the hematological recovery and adverse events. Eligible responders could proceed to allogeneic stem cell transplantation (alloSCT). We evaluated baseline characteristics, IPSS-R, IPPS-M values, marrow CR (mCR), CR, CRi rates, overall survival (OS), time to ANC>$1x10^9$ and PLT>$100x10^9$ recovery from the start of the treatment, CTCAE v5.0 grade 3-5 non-hematological toxicity, day-30, day-60 mortality rates.

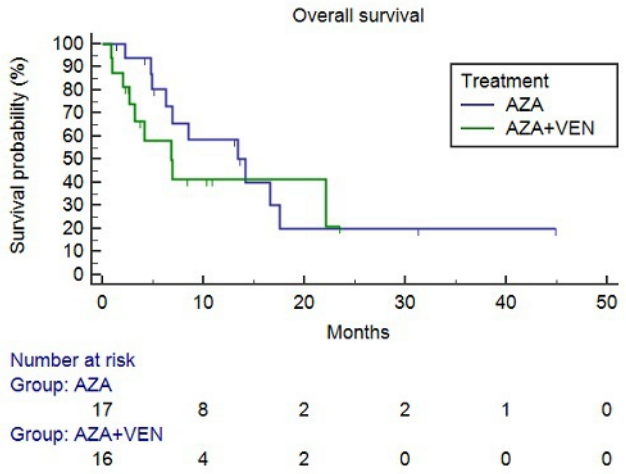
Results:

16 patients (10 female) were treated with AZA+VEN whereas 17 (7 female) patients received AZA. Median age and ECOG values were 59 years (38-71) and 1 (0-2) in the AZA+VEN cohort compared to 74 years (53-84) and 2 (1-3) in the AZA group, respectively (p<0.001, p=0.026). The median IPSS-R value was 7.5 (5-10) in the AZA+VEN group and 6 (5-8) in AZA patients (p=0.004). The median IPSS-M value was 2.57 (0.55-4.57) in the AZA+VEN group, whereas data was not available for AZA patients. Complex karyotype was identified in 5/16 (31%) and 3/17(18%) in AZA+VEN and AZA patients, respectively (p=0.438). A median of 1 (1-3) AZA+VEN treatment cycle was administered, whereas AZA was given for a median of 4 (1-27) cycles. The mCR rate was 12/15 (75%) in the AZA+VEN patients and 6/15 (40%) in the AZA group (p=0.06). The CR+CRi rate was 9/15 (60%) in the AZA+VEN group in comparison to 5/15 (33%) in the AZA patients (p=0.272). 5/16 (31%) of AZA+VEN patients were bridged to alloSCT, whereas none of the AZA was allotransplanted. The median follow-up was 10.3 months in the AZA+VEN cohort and 31.3 months in the AZA group. The median OS was 6.8 months (3.2-22.1) and 14.1 months (6.9-17.6) in the AZA+VEN and AZA groups, respectively (p=0.436). 2-year OS was 20% in both groups

(Figure 1). The median time to ANC and PLT recovery was 50 (4-165) and 60 days (21-94) in the AZA+VEN cohort compared to 38 (35-74) and 48 days (28-129) in AZA patients, respectively (p=0.66, p=0.464). Grade 3-5 adverse events occurred in 7/16 (44%) of AZA+VEN patients in comparison to 7/17 (41%) in the AZA group (p=0.881). Day-30 and day-60 mortality rates were 2/16 (13%) and 3/16 (19%) in the AZA+VEN group. No early deaths occurred in the AZA cohort.

Summary/Conclusion:

AZA+VEN treatment demonstrated higher response rates in MDS-IB2 patients however, this did not translate into prolonged survival compared to AZA monotherapy. Trends toward longer hematological recovery and higher early mortality were evident in the AZA+VEN group. Nevertheless, our real-life results should be interpreted with caution due to the small patient numbers, significant intergroup differences, and the retrospective nature of the study.



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