PB1840 MONOCENTRIC EXPERIENCE OF VENETOCLAX-BASED REGIMENS FOR ACUTE MYELOID LEUKEMIA

Topic: 04. Acute myeloid leukemia - Clinical

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Background:

Combination of venetoclax and hypomethylating agents (HMAs) has become a standard of care in adult patients with acute myeloid leukemia (AML) who are aged>75 years or who have comorbidities that preclude use of intensive induction chemotherapy. Few promising data are available in the setting of relapsed/refractory (R/R) AML, while the utility of venetoclax in the post-transplant setting remains poorly investigated.

Aims:

To investigate clinical outcome and safety of venetoclax-based combinations in AML patients treated outside of clinical trials.

Methods:

We conducted a monocentric retrospective analysis on adult patients affected by treatment-naïve AML not eligible for standard induction therapy or R/R AML, who started venetoclax combination regimens between November 2017 and December 2021. AML genetic risk stratification and response criteria were assessed according to 2017 European Leukemia Net (ELN) consensus. Venetoclax was administered at the dose of 400 mg daily after a short ramp-up. The venetoclax dosage was reduced to 50 or 100 mg daily in case of concomitant strong CYP3A4 inhibitors (e.g. posaconazole) and 200 mg daily in case of moderate CYP3A4 inhibitors (e.g. isavuconazole). Disease free survival (DFS) and overall survival (OS) were assessed using the Kaplan-Meier method and compared between groups using the log-rank test; p values <0.05 were considered significant.

Results:

A total of 60 consecutive AML patient treated with venetoclax-based combinations were considered in the study. Twenty-three patients (38%) were affected by treatment-naïve AML and 37 patients (62%) by R/R AML. The median age was 70 years and 67% of the patients were >65 years old. The majority of patients showed an intermediate ELN genetic risk, while adverse ELN risk was found in 39% of treatment-naïve patients and 32% of R/R group. Among patients with R/R AML, 62% were treated in the salvage-2 setting or later and 37% had received a prior allogenic stem cell transplantation (allo-SCT). In combination with venetoclax, 51 patients (85%) received azacitidine 75 mg/m2 days 1-7. Eight patients (13%) added venetoclax to HMAs after progression during hypomethylating treatment previously administered for pre-leukemic conditions. Antifungal prophylaxis and subsequent venetoclax dose reduction were performed in 32 patients (53%). Overall response rate was 60% with a complete remission (CR) rate of 53% (78% for treatment-naïve group and 49% for R/R group, p 0.017). The best response was achieved after a median of one months. Median OS was 130 days for R/R patients and 269 days for treatment-naïve patients; median DFS was 199 days for treatment-naïve patients and 145 days for R/R cohort. Genetic adverse risk had a significant worst survival (p 0.02, Figure 1). Among patients who were treated after allo-SCT venetoclax lead to a CR rate of 36%. Overall, 11 patients (18%) received an allo-SCT after venetoclax combinations (7 as consolidation of a first line therapy). Most common grade 3 or 4 adverse events were hematological or infectious toxicities (31% and 64%). One event of severe tumor lysis syndrome was reported.

Image:
Summary/Conclusion:

The results of this real-life monocentric study confirmed that venetoclax-based regimens are a viable and safe option as first-line therapy for AML unfit patients and a valid rescue therapy in the R/R setting. Furthermore, the association of venetoclax and hypomethylating agents proved to be a feasible bridging therapy to transplantation in elderly AML patients.