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POSTER ABSTRACTS

615.ACUTE MYELOID LEUKEMIAS: COMMERCIALLY AVAILABLE THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Outcomes and Hospital Resource Utilization Associated with Decreased Ven Exposure in Acute Myeloid Leukemia Patients: A Real-World Retrospective Review

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Patients (pts) with acute myeloid leukemia who are ineligible for intensive chemotherapy are treated with hypomethylating agent (HMA) and Venetoclax (Ven). We previously reported outcomes on a cohort of our pts hospitalized for induction therapy demonstrating that the majority of pts required Ven exposure de-escalation. Despite its widely accepted clinical practice, no prospective study has evaluated the efficacy in retaining remission or the tolerability of less Ven exposure per cycle (cyc). Additionally, there is no study evaluating the effect of delaying treatment secondary to its myelosuppressive toxicities. We aim to present outcome data on a large cohort of all AML pts treated with HMA + Ven within our healthcare system.

We queried Northwell Cancer Institute's electronic health records to identify all pts with AML who received at least one cyc of Ven and HMA between January 2019 and December 2022. Groups for analysis were created for pts who received at least 3 cyc of HMA and Ven based on the median Ven exposure days per cyc (≤ 14 days or ≥ 15 days) and the median days between cyc (≤ 34 or ≥ 35 days) excluding cyc 1 and 2. Median relapse-free survival (mRFS) and median event-free survival (mEFS) in months (m) were defined by ELN 2022 criteria. Pts who received allogeneic transplants (n=4) were excluded from survival evaluations. Kaplan-Meier (KM) method and log rank testing was used to compare time to event data.

We identified 142 AML pts who received at least 1 cyc of Ven + HMA. Pts had an ORR of 42%, mEFS of 4m and mOS of 9.6m. The median age was 77. Only 76 pts received 3 or more cyc of HMA + Ven with mRFS 11.6m of and mOS of 20.6m. Of these pts, 39 had AML with myelodysplastic changes, 29 had *De Novo* AML and 8 had secondary AML. 75% of pts received HMA + Ven as first line treatment. Utilizing the 2022 ELN risk categories (Dohner et al, Blood 2022), 12 had favorable risk, 12 had intermediate risk and 52 had adverse risk. 93% had treatment regimen modifications by either reduced Ven/cyc or increased cyc intervals. All prognostic indicators appeared evenly dispersed among the groups.

Pts with ≤14 days of Ven/cyc (n=35) had a median of 7 cyc (range 3-24) and remained on treatment for a median of 11.3 m. Meanwhile, pts with ≥15 days/cyc (n=41) had a median of 5 cyc (range 3-24) with a median of 10.1m on treatment. The ≤14 days of Ven/cyc group had significantly improved RFS (15.8m vs 8.7m) and OS (24.7m vs 11.3m) compared to the group of pts receiving ≥15 days/cyc ($p < 0.01$). Additionally, there was a decrease in number of hospital days, RBC and platelet transfusions in this group compared to the ≥15 days/cyc group (figure 2).

66% of pts (n=50) required increased time interval between cycles. Both ≤ 34 and ≥ 35 days cyc interval groups completed median of 6 cyc. No significant difference was found in mRFS (11.6m vs 11.8m) or mOS (15.1m vs 21.8m). However, there was a reduction in hospital days, pRBC and platelet transfusions in the ≥ 35 day interval group (figure 2).

The overall response rate, mRFS and mOS of all 144 patients seem to be decreased compared to reported prospective trials. This may be due to differences in frailty in our pt population. Although limited by the bias of retrospective analyses, our evaluation of pts outcomes demonstrates a statistically and clinically significant improvement in mRFS and mOS in pts with decreased Ven days/cycle. The majority of pts had Ven/cycle decreased by cycle 3 and most were intermediate or high risk. Our results also highlight the decrease in hospital resource utilization and transfusion needs in this group which may lead to improved quality of life and decreased costs. The ≤14days Ven/cycle group had improved survival compared to the VIALE-A and DEC10-VEN trial despite a larger proportion of our pts having adverse risk. We hypothesize that this improvement

is likely multifactorial secondary to decreased mortality from higher Ven exposure, improved tolerance causing increased HMA exposure from timely dosage and from a theoretically possible decreased intracellular adaptive mechanisms generating resistance from continuous Bcl-2 inhibition. This emphasizes the need for continued reporting of outcomes of therapy with HMA/Ven. Additionally, due to the clinically significant improvement in mRFS and mOS, a prospective trial evaluating the efficacy, tolerability, and impact on quality of life of reduced Ven exposure/cyc should be considered.

Disclosures No relevant conflicts of interest to declare.

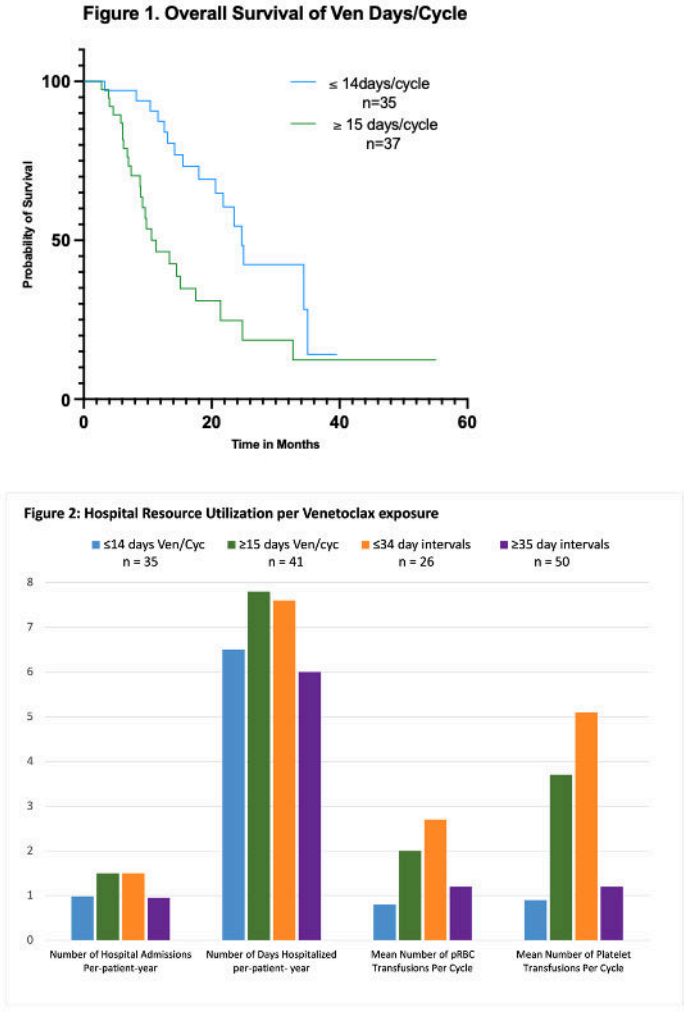

Figure 1

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