Quality Assurance Evaluation of Venetoclax and Hypomethylating Agents in Acute Myeloid Leukemia

Cameron Hallisey (hallisey@usc.edu)

Background/Purpose: Acute Myeloid Leukemia (AML) is an aggressive form of leukemia with limited treatment options in elderly populations. Venetoclax (VEN) is an oral antineoplastic drug approved for use in combination with hypomethylating agents (HMA) azacitidine or decitabine in the setting of AML. The primary objective of this study is to assess the risks and benefits of truncated VEN dosing often seen in practice.

Methods: The Institutional Review Board (IRB) approved this retrospective, single site, cohort study at Cedars-Sinai Medical Center (CSMC). Adult patients (18+) diagnosed with AML were included if they received VEN-HMA or HMA-monotherapy regimens and excluded if they opted out of research participation. Participants (n = 84) were assigned to HMA-monotherapy and 3 VEN-HMA treatment groups (1-7, 8-14, 15+ days of VEN). The primary efficacy endpoint is the number of cycles to response (CR, CRi, CR MRD+, CR MRD-). Secondary endpoints include the incidence of febrile neutropenia, duration of neutropenia, and survival. Statistical analysis was performed using one-way ANOVA tests and Kaplan Meier survival tests.

Results: The mean number of cycles to response was similar, with the HMA-VEN 8-14d group having the lowest average of 1.33 cycles. VEN-HMA treatment groups showed increased 1-year median survival rates in comparison to the HMA monotherapy group ($p= 0.0043$). While there was no difference in incidence or duration of neutropenia between the groups, there was a trend towards increased incidence of febrile neutropenia in the VEN treatment groups.

Conclusions: This data supports the use of VEN-HMA combination therapy over HMA monotherapy in the setting of AML, as well as the use of truncated dosing regimens that we see in practice. The VEN-HMA regimens with 8-14 days of VEN per cycle may be ideal for achieving CR while minimizing the adverse effects. Additional studies are needed to determine if there is an optimal duration of VEN in combination with HMAs for AML.