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General AML

Venetoclax combined with HMAs or LDAC is a viable salvage option in patients with R/R AML

 **Anna Bartus**  **Cynthia Umukoro** | Jan 23, 2018

In the December 2017 issue of the American Journal of Hematology, Courtney D. DiNardo from the University of Texas MD Anderson Cancer Center (MDACC), Houston, TX, and colleagues published results of their study, which aimed to determine the efficacy and safety of venetoclax (VEN [an oral, selective BCL2 inhibitor]) combination strategies in the salvage setting in patients with Relapsed/Refractory (R/R) Acute Myeloid Leukemia (AML) and/or associated myeloid malignancies including Myelodysplastic Syndromes (MDS) and Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN).

In total, 43 patients (median age = 68, range, 25–83 years) with R/R AML (n = 39), MDS (n = 2) or BPDCN (n = 2), who were treated with VEN salvage combination regimens between 10 June 2016 and 6 July 2017 at the MDACC were analyzed in this study. Patients received ≥ 14 Days of VEN with either Hypomethylating Agents (HMAs), azacitidine (n = 8) or decitabine (n = 23) or Low-Dose Cytarabine (LDAC [n = 8]) or other (n = 4).

Key findings:

- Response
  - Objective Response Rate (ORR) in all patients: 21% (9/43)
    - Complete Response (CR) = 5% (2/43)
    - Morphologic Leukemia-Free State (MLFS) = 9% (4/43)
  - Median Overall Survival (OS) in all patients: 3.0 months (range, 0.5 – 8.0)
  - Median OS in responding patients (n = 9): 4.8 months
  - ORR in patients with diploid/intermediate risk cytogenetics: 24% (5/21)
  - ORR in patients with *IDH* mutations: 21% (3/11)
    - Peripheral blast clearance within the first two weeks of treatment was observed in one IDH mutated patient
    - One IDH mutated patient experienced > 50% bone marrow blast reduction without peripheral count recovery
  - ORR in patients with *RUNX1* mutation: 50% (4/8)
  - ORR in *TP53* mutated patients: 20% (2/10)
  - ORR in patients with adverse risk cytogenetics, all with concurrent *RUNX1* mutation: 15% (3/20)
- Safety
  - Grade >3 neutropenia occurred in all patients receiving VEN combination therapy

- Most common grade > 3 documented infections during treatment occurring in 72% of patients include pneumonia (40%), gram-negative bacteremia (30%), gram-positive bacteremia (23%), cellulitis (21%), invasive fungal infection (19%) and urinary tract infections (14%)
- Discontinuation occurred in 38 patients due to no response/ progressive disease (n = 29), death (n = 7) or transition to transplantation (n = 2)

In summary, this is the first study to report on the "effectiveness of VEN combination strategies for R/R myeloid population". The authors stated that their findings demonstrate that low-dose chemotherapy either with HMAs or LDAC, in combination with VEN is a "viable salvage treatment" and provides an alternative therapy option for patients with R/R AML, MDS, and BPDCN. Moreover, responses were observed in patients with diploid/intermediate cytogenetics, *RUNX1*, and/or *IDH1/2* mutations.

References

1. DiNardo C.D. *et al*. Clinical experience with the BCL2-inhibitor venetoclax in combination therapy for relapsed and refractory acute myeloid leukemia and related myeloid malignancies. Am J Hematol. 2017 Dec 8. DOI: 10.1002/ajh.25000. [Epub ahead of print]