Treatment of Pracinostat and Azacitidine in Elderly Patients With Acute Myeloid Leukemia (AML): Correlation Between Mutation Clearance and Clinical Response

Koichi Takahashi, Yasmin Abaza, Feng Wang, Curtis Gumbs, Song Xingzh; Andrew Futreal, Ehab Atallah, Bruno C. Medeiros, Samer K. Khale; Martha Arela; Minin M. Patnaik; Elena Palermo; Guilermo Garcia-Marone

University of Texas MD Anderson Cancer Center, Houston, TX, USA; Department of Hematology/Oncology, Medical College of Wisconsin, Milwaukee, WI, USA; Department of Medicine, Division of Hematology, Stanford University, Stanford, CA, USA; Department of Hematology and Hematopoietic Cell Transplantation, and Gehr Family Center for Leukemia Research, City of Hope, Duarte, CA, USA; University of Miami School of Medicine, Division of Hematology, Miami, FL, USA; Mayo Clinic, Division of Hematology, Rochester, MN, USA; Helsinn Healthcare, Lugano, Switzerland

BACKGROUND

- Older patients with acute myeloid leukemia (AML) have poor prognosis, with a median overall survival (OS) of 5–10 months.
- A better understanding of the genetic aberrations and their association with patient outcomes, as well as more effective and better-tolerated treatments, is needed for AML.

METHODS

Study Design
- The phase 2 study evaluated the combination of pracinostat and azacitidine in 50 patients aged ≥65 years with previously untreated AML who were not eligible for intensive care regimens.
- Patients were treated with pracinostat 75 mg/m² administered daily intravenously/subcutaneously and azacitidine 75 mg/m² administered daily intravenously/ subcutaneously for 7 days. Treatment cycles were repeated every 28 days.

Patient Population
- Key inclusion criteria: Age ≥65 years; newly diagnosed acute AML, secondary AML, or de novo AML with 30% or more blasts.
- Exclusion criteria: Prior HDAC inhibitor or deacetylase inhibitor; active central nervous system disease.

RESULTS

Demographics and disease characteristics were comparable in the study population. The phase 2 study evaluated the combination of pracinostat and azacitidine in 50 patients aged ≥65 years with previously untreated AML who were not eligible for intensive care regimens. A CR was achieved in 10/19 patients who had longitudinal sequencing analysis and at the time of CR, 9/10 had persistently detectable mutations in their bone marrow.

CONCLUSIONS

- Mutations in APM1 and the DNA methylation pathway were common in the study population and associated with a better response to pracinostat and azacitidine, while TP53 mutation was associated with a poor response.
- —Mutations that respond to pracinostat and azacitidine may be an important factor in the favorable OS and CR findings in the overall study.
- Persistent mutation at the time of CR suggests residual leukemic clonal hematopoeis.
- Continued treatment increases the rate of minimal residual disease clearance as defined by decline of mutation VAF after achieving CR.

REFERENCES: