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## Strategies for Achieving Durable Responses in Elderly AML Patients

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Welcome to *Managing AML*, I am Dr. Keith Pratz, and I will be reviewing an abstract presented at the European Hematology Association's Annual Congress: Durable response with venetoclax in combination with decitabine or azacitidine in elderly patients with acute myeloid leukemia.

This is data presented updating some earlier results of the phase 1B study where venetoclax is being added to induction therapy with the backbone of decitabine or azacitidine in patients who are unfit for conventional induction chemotherapy. This summarized the outcomes of 145 patients with a median age of 74 who were diagnosed with acute myeloid leukemia and who had not received prior therapy. The patients were a mix of patients with intermediate and unfavorable karyotypes, and patients could also have had secondary acute myeloid leukemia. The breakdown of the patients was such that half of the patients received decitabine and half of the patients received azacitidine as backbone therapy, and two different dose levels of venetoclax – 400 mg and 800 mg – were studied. Patients received venetoclax starting on day 1 with a ramp-up of dosing up to the target level of 400 mg or 800 mg, and patients were followed for tumor lysis for the first three to four days while the dose ramp-up was occurring.

Adverse events experienced on the study were typical of those seen with acute myeloid leukemia therapy; most commonly, febrile neutropenia and thrombocytopenia, as well as low white blood cell count were noted. Patients tolerated therapy quite well with an early death rate of only 3% in the first 30 days of treatment, and 8% within 60 days of starting therapy. The responses seen on the study were quite favorable in that 67% of patients overall achieved a complete response (CR) or complete response with incomplete blood count recovery (CRi) on the study. Broken down by subgroup analysis, at the phase 3 dose of venetoclax 400 mg daily along with azacitidine, there was a CR/CRi rate of 76%. The authors also presented some minimal residual disease data showing that in those patients who achieved CR or CRi via conventional criteria, approximately one-third of those patients were negative via a multi-flow cytometry MRD assessment.

How these results impact current management of acute myeloid leukemia is yet to be determined as there is a phase 3 study evaluating the combination of venetoclax and azacitidine versus azacitidine alone which has finished accrual and we are awaiting results of. If the results in that study show responses at this level, one might suspect that this would become a standard way in which elderly patients are treated for acute myeloid leukemia. As I

mentioned, that phase 3 study has completed accrual and we are eagerly awaiting those results; the trial is structured to observe an overall survival benefit in the favored arm.

The key points that the audience should take away here are that patients are achieving a high level of responses with venetoclax and azacitidine with a median survival of 15.6 months of follow-up. The observed median overall survival was 17.5 months, with approximately 50% of those patients showing an overall survival at one year.

Thank you for viewing this activity.

#### **ABSTRACT**

DiNardo CD, Pratz K, Potluri J, et al. Durable Response with Venetoclax in Combination with Decitabine or Azacitidine in Elderly Patients with Acute Myeloid Leukemia (AML). EHA23: 2018. Abstract: S1563.

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