**The Clinical Challenge of Older AML Patients Ineligible for Intensive Chemotherapy: Clinical Trial Results of Venetoclax in Combination with Cytarabine and HMAs**

**Daniel A. Pollyea, MD**
Clinical Director of Leukemia Services
Associate Professor of Medicine
Division of Hematology
University of Colorado
Denver, Colorado

***285. Venetoclax in Combination with Hypomethylating Agents Induces Rapid, Deep, and Durable Responses in Patients with AML Ineligible for Intensive Therapy***

Hi. I am Dan Pollyea, and I am here at the 60th Annual ASH Meeting. I am very excited to discuss with you an abstract. The first abstract is *Venetoclax in Combination with Hypomethylating Agents Induces Rapid, Deep, and Durable Responses in Patients with AML Ineligible for Intensive Therapy*.

This abstract was, I think, really important because it looks at that age cohort, older AML patients, which is the majority of patients, who in this case were not deemed fit for intensive induction chemotherapy. They were given venetoclax with azacitidine or decitabine backbone therapies, and we have previously presented and reported on this data, what makes this abstract different is that we really focused on the 400 mg dose cohorts of venetoclax, which is the dose cohort that was recently FDA approved. In this setting, with venetoclax and azacitidine and venetoclax and decitabine, always with 400 mg of venetoclax, we are seeing very high response rate, so in the order of 70% with both azacitidine and decitabine. With that, we are seeing quite durable responses, so the median duration of therapy with an ongoing clinical trial is looking very promising, as well as overall survival. At the moment, again, with an ongoing clinical trial, we are looking at an overall survival with either azacitidine or decitabine on the order of 17 months. The nice thing about this therapy is that there are not particular genomic subgroups that at least with relatively small numbers seem to respond worse. This regimen really does work for across the board AML patients regardless of genomic or cytogenetics, and we are also able to get MRD negativity in a fair number of the patients, so the responses are quite deep. We are really excited about this now FDA-approved therapy and I think this data helps us understand a little bit more what to expect and how to have these discussions with patients.

**Reference:** Pollyea D, Pratz K, Jonas B. et al. Venetoclax in Combination with Hypomethylating Agents Induces Rapid, Deep, and Durable Responses in Patients with AML Ineligible for Intensive Therapy. ASH 2018. Abstract 285.

***284. Venetoclax with Low-Dose Cytarabine Induces Rapid, Deep, and Durable Responses in Previously Untreated Older Adults with AML Ineligible for Intensive Chemotherapy***

This abstract is *Venetoclax with Low-Dose Cytarabine Induces Rapid, Deep, and Durable Responses in Previously Untreated Older Adults with AML Ineligible for Intensive Chemotherapy,* and this abstract was presented by Steve Strickland from Vanderbilt University.

This continues the experience we have with venetoclax with backbone therapies in the untreated, deemed unfit for intensive chemotherapy older AML patients. In this setting, using 600 mg of venetoclax with low-dose cytarabine, we now have more mature data and more experience with response rates. Response rates are high, on the order of 60%, with a lot of these responses being complete remissions. Responses appear to be quite durable and with early follow-up timepoints, overall survival looks also very promising. This backbone therapy is often compared to the hypomethylator study which was also presented at this year's ASH. One of the major differences between these two presentations is that patients who enrolled in the low-dose cytarabine backbone therapy could have had a prior hypomethylator if they had MDS, for instance. Whereas those patients would have been excluded from the hypomethylator backbone therapy that was also presented. And 40% of the patients actually did have this prior exposure to hypomethylator and Steve presented that the patients who had that prior exposure to a hypomethylator did not do as well as the patients who are truly untreated. That may account for the slight difference in response rates with respect to this backbone therapy compared to hypomethylators. But regardless, this therapy was recently FDA approved, so 600 mg of venetoclax and low-dose cytarabine for a newly diagnosed AML patients, older and unfit for intensive chemotherapy, and it is a very exciting new strategy that takes advantage of venetoclax, and I think will offer a lot of very hopeful options for patients.

**Reference:** Wei A, Strickland S, Hou J, et al. Venetoclax with Low-Dose Cytarabine Induces Rapid, Deep, and Durable Responses in Previously Untreated Older Adults with AML Ineligible for Intensive Chemotherapy. ASH 2018. Abstract 284.