

## **Abstract: PB2505**

### **Title: HYPOMETHYLATING AGENTS + VENETOCLAX THERAPY IN LATE ELDERLY AML: “TO BE OR NOT TO BE” WELL EFFECTIVE?**

**Abstract Type: Publication Only**

**Topic: Acute myeloid leukemia - Clinical**

#### **Background:**

Acute myeloid leukemia (AML) is a disease that particularly affects the elderly population, numerous epidemiological studies show that approximately 1/3 of patients (pts) with AML are aged >75 years (y).

Since 2020, the association of hypomethylating agents (HMA) with venetoclax has increased efficacy of the less-intensive therapeutic options.

The real-world data of this association in a strictly late elderly population are scarce and fragmented even though they represent a crucial issue for improving the optimization of therapeutic choices.

#### **Aims:**

The aim is to observe feasibility in terms of tolerance and safety, as well as efficacy, of the association of HMA+venetoclax in late elderly population (>75 y).

#### **Methods:**

We retrospectively collected data from all >75 y AML pts treated with HMA+venetoclax at our center from 2020, outside clinical trials. We considered diagnoses, risk stratification and responses according to ELN 2022. Overall Survival (OS) and Event-free Survival (EFS) were obtained using Kaplan-Meier method. Significant p-value was expressed as <0.05.

#### **Results:**

We considered 26 pts with a median age of 80.3 y (range 75.6-90.1). All other clinical features are summarized in Figure 1A.

The most common regimen was azacitidine+venetoclax vs decitabine+venetoclax in 15 (58%) and 11 (42%) pts, respectively. In 6 cases (23%) HMA+venetoclax was utilized as second line of treatment. Total number of cycles for each pts ranged from 2 to 31.

Best response (BR) was not evaluable in 2 pts; 11 pts had no response (46%), 2 had partial response (PR) (8%), other 2 a Morphologic Leukemia-Free State (MLFS) (8%), 3 had complete response (CR) with partial hematologic recovery (CRh) (13%) and in the further 6 pts CR was obtained (25%). The median time to achieve BR was 2.8 months (range 1.3-6.9), in most cases after two cycles (9 pts, 37.5%). The only factor that has a statistical correlation with the response is the previous treatment with HMA: 5/6 pts (83.3%) previously exposed to HMA, in opposition to 6/18 (33.3%) not previously treated (p 0.033), did not obtain response.

Mean follow-up was 7.8 months (range 1-35.7). Figure 1B-C represents EFS (as death, progression, or interruption) and OS. The median EFS and OS was reached at 5.8 and 6.3 months, respectively.

Variables influencing OS were risk class and type of BR according to ELN2022, with advantage of favorable risk and complete response: in both cases the median OS was not reached (p 0.011 and 0.026, respectively). (Figure 1D-E)

Safety was good: no interruption due to toxicity occurred, the only noteworthy data is that in 11 pts (42%) it was necessary to postpone the second cycle mainly due to neutropenia (8 pts).

**Summary/Conclusion:**

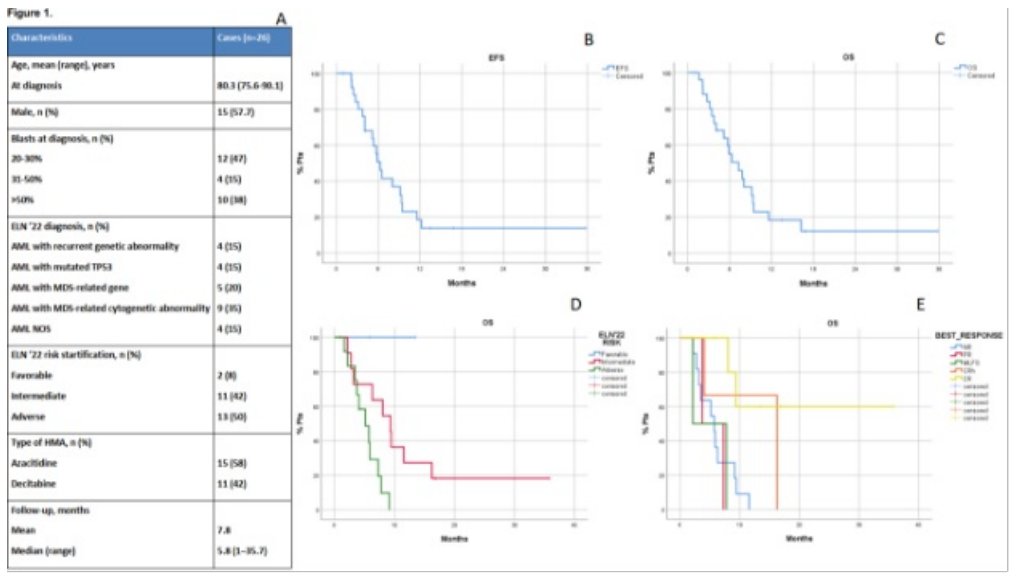
Regarding the late elderly treated with HMA+venetoclax, no other real-world series have yet been published. With the limitations of retrospective analysis, we can say that this approach is feasible also in this setting.

Not considering patients previously treated with HMA response rates were meaningful already after two cycles. The depth of responses positively influenced long-term survival.

The latest ELN2022 risk classification showed to be effective in predicting OS in this subpopulation as well.

Remarkably, a similar trend of EFS and OS underlines the importance of the first line of treatment because the loss of response or progression often coincides, in fact, with the rapid death of the patient.

Obviously, only further studies, possibly prospective, will be able to highlight the superiority of regimens based on HMA+venetoclax compared to best supportive care.



**Keywords:** Venetoclax, Elderly, AML, Hypomethylating agents