Impact side effects of specific therapy in combination with venetoclax on outcome in patients with acute myeloid leukemia

Sokalav-Varapayev, Alexey[1]; Lendina, Irina[2]; Iskrov, Ihar[3]

[1]Minsk Scientific and Practical Center for Surgery, Transplantology and Hematology, Minsk, Belarus, monkey192@mail.ru; [2]Minsk Scientific and Practical Center for Surgery, Transplantology and Hematology, Minsk, Belarus, haematology3@gmail.com; [3]Belarusian State Medical University, Minsk, Belarus, gemotol@mail.ru

Introduction. One of the targeted drugs used to treat acute myeloid leukemia (AML) is venetoclax, a selective inhibitor of the antiapoptotic protein BCL-2. In a study by Mohamed Jiffry M.Z. et al, venetoclax in the treatment of patients with resistant AML provides a survival benefit comparable to that seen in patients with primary AML. In a multicenter, randomized, double blind, placebo-controlled study, DiNardo et al found that the most common serious complications of the combination of azacitidine with venetoclax are thrombocytopenia grade 3–4, neutropenia and infections.

Objectives. To study the incidence of adverse reactions of specific therapy with a combination of venetoclax in patients with AML and to affect the impact side effects on outcome in patients with acute myeloid leukemia.

Materials and methods. The prospective cohort study included 22 adult patients with AML who received specific therapy in combination with venetoclax from November 2022 to October 2024 on the basis of the hematology department №3 of the Minsk Scientific Practical Center of Surgery, Transplantology and Hematology. Microsoft Excel 2016 and R Studio 2024.09.0 were used for statistical data analysis. The overall survival of the study group was estimated using the Kaplan-Meier method. Analysis results were considered statistically significant at $p < 0.05$.

Results. The age of the patients ranged from 24 to 80 years (median — 61.5 years), among them there were 14 women (63.6 %) and 8 men (36.4 %).

All patients, depending on clinical and laboratory status, were prescribed venetoclax in combination with hypomethylating agents, low doses of cytarabine or ruxolitinib, 3 patients (13.6 %) received specific therapy in combination with venetoclax as the first line at the diagnosis of AML, 19 patients (86.4 %) in relapsed and refractory forms of AML.

Remission was achieved in 9 patients with AML (41 %), of which transplantation was performed in 4 patients (18.1 %), relapses during combination therapy with venetoclax were reported in 3 patients (13.6 %).

Due to serious side effects (stage 3–4 thrombocytopenia, neutropenia and infection), courses with the addition of venetoclax were interrupted in 16 patients (72.7 %), among them — in 14 patients in 87.5 % of cases due to infectious complications.

At the time of analysis the death was reported in 9 AML patients (41 %). The results of overall 2-year survival in the groups of patients with the presence and absence of complications during specific therapy in combination with venetoclax were presented in Figure 1.

Overall survival in the cohort of patients with complications was 43.8 %, the median overall survival was 20.8 months. Overall survival in the cohort of patients without complications was 100 %, the median overall survival was not achieved. There are differences in survival between the complication cohort and the non-complication cohort ($p = 0.038$).

Conclusion. Thus, the presence of serious side effects during specific therapy with a combination of venetoclax statistically significant affects the survival of patients with AML.

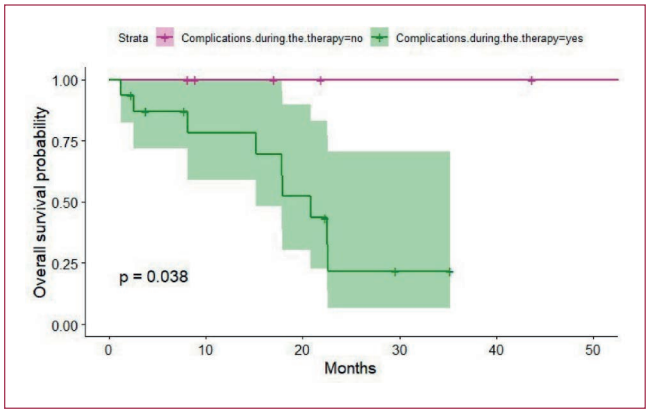

Figure 1. Overall survival on venetoclax-supplemented therapy depending on the presence of complications