P1221 DIFFUSE LARGE B-CELL LYMPHOMA RICHTER SYNDROME IN CHRONIC LYMPHOCYTIC LEUKEMIA – A RETROSPECTIVE ANALYSIS OF TREATMENT OUTCOMES IN POLISH ADULT LEUKEMIA STUDY GROUP

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

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Background: Richter syndrome (RS) is a recognized uncommon manifestation and evolution of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) with a dismal prognosis. It occurs in 2-10% of CLL patients. It is associated with a clonal evolution and progression, generally with a transformation of the original CLL clone to diffuse large B-cell lymphoma (DLBCL) or, less frequently, to Hodgkin Lymphoma (HL). Despite the advances in understanding pathogenesis of the disease, the DLBCL variant of RS (DLBCL-RS) is associated with a dismal prognosis with a median survival < 1 year. The treatment options and risk factors of worse outcome for RS still need to be further expanded.

Aims: To study the characteristic and treatment outcomes of patients with DLBCL-RS.

Methods: The retrospective analysis of 99 patients diagnosed with DLBCL-RS treated in hematology centers of the Polish Adult Leukemia Study Group (PALG) between 2011 and 2021.

Results:

Clinical data of 124 patients with Richter syndrome was collected. Ninety-nine patients were diagnosed with DLBCL-RS (79.8%) and further analyzed. Median time since CLL diagnosis to Richter transformation was 43.0 months (range 0-252.0). At the time of transformation 31.3% patients had CLL Rai stage IV, 74.7% were ECOG< 2, while the median Cumulative Illness Rating Scale (CIRS) was 4 (range 0-16). Thirty-seven patients transformed during CLL treatment, 56.7% of them were receiving novel agents (Brutons tyrosine kinase inhibitor or BCL2 inhibitor). Median time of observation after transformation was 10.7 months (range 0-98.6). Median overall survival (OS) after DLBCL-RS diagnosis was 17.3 months (95% CI 11.9-46.8) and median progression-free survival (PFS) 13.5 months (95% CI 9.6-22.7). Seventy-six patients (76.8%) had RS treated with intensive chemotherapy protocols, mainly R-CHOP-like regimens for the first line treatment. Only 42.3% had response to the treatment (25/76 complete responses and 11/76 partial responses). Worth mentioning is that in the group of patients with response two patients had ibrutinib monotherapy and one had rituximab-ibrutinib.

In forty patients RS was primarily resistant to administered treatment and 65% of them died due to progression or treatment related complications. In the primary resistant DLBCL-RS p53 pathway aberration was noted in 47.5% of
patients (17p deletion in 13 patients or TP53 mutation in 6 patients). Better results were achieved for patients who proceeded to autologous hematopoietic stem cell transplantation (auto-HSCT; n=8) and allogeneic HSCT (allo-HSCT; n=10). The median OS in auto-HSCT recipients was 46.1 months, while in allo-HSCT the median OS reached 18.3 months (3 patients died due to allo-HCST-related complications). Significantly lower OS (3.4 months, 95% CI 14.13-not reached) was observed for RS in heavily pretreated CLL patients (>3 lines of therapy preceding transformation) compared to those treated with up to 3 lines of therapy (23.7 months) (p=0.0002). Median OS for treatment naïve patients at DLBCL-RS diagnosis was not reached. Other factors identified as predictors of poor OS in univariate analysis were ECOG ≥2 (p=0.0014), hemoglobin level <10 g/dl (p=0.017) and platelet count <100x10^9/L (p=0.0065).

**Summary/Conclusion:**

Our study represents the largest dataset of DLBCL-RS patients in Polish hematology centers and confirms the poor outcomes and prognosis associated with RS. The worst treatment results were observed in RS receiving >3 lines of CLL therapy preceding transformation. Only proceeding to hematopoietic stem cell transplantation may improve the prognosis.