

# Multicenter International Experience in the Treatment of Aggressive Peripheral T-Cell Lymphomas

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## Introduction

Peripheral T-cell lymphomas represent a rare and morphologically heterogeneous group of predominantly aggressive mature T/NK-cell neoplasms characterized by a high frequency of primary refractory disease and relapse. We conducted a multicenter analysis of therapy in patients with aggressive peripheral T-cell lymphomas, taking into account the use of hematopoietic stem cell transplantation as well as targeted and immunotherapy.

## Patients and Methods

The study included 204 patients with aggressive variants of peripheral T-cell lymphomas. Histological distribution was as follows: peripheral T-cell lymphoma, not otherwise specified — 33%; anaplastic large-cell lymphoma ALK+ — 15%; anaplastic large-cell lymphoma ALK- — 19%; angioimmunoblastic T-cell lymphoma — 17%; and other rare forms — 16%. The median age was 47 years (range 1–76), and the median follow-up for surviving patients was 46 months (range 7–234). Primary refractory or relapsed disease was observed in 172 patients (84%). Autologous hematopoietic stem cell transplantation was performed in 79 patients, and allogeneic hematopoietic stem cell transplantation in 28 patients. In 76 cases (37%), targeted and immunotherapy were administered based on the biological features of the tumor.

## Results

Five-year overall survival and progression-free survival for the entire cohort were 49.5% and 32.4%, respectively. Subgroup analysis of first-line therapy demonstrated the benefit of consolidating the initial chemosensitive response with autologous hematopoietic stem cell transplantation (progression-free survival 57.9% versus 21%;  $p = 0.024$ ). Comparison of autologous hematopoietic stem cell transplantation performed in first versus subsequent lines of therapy showed five-year progression-free survival rates of 60% and 37%, respectively ( $p = 0.026$ ). Experience with targeted and immunotherapy demonstrated overall response rates of 48% for brentuximab vedotin monotherapy and 52% in combination, 50% for nivolumab monotherapy and 22% in combination, and 83% for ALK inhibitors in monotherapy and 100% in combination. Among 15 patients (60%) with chemoresistant disease who underwent allogeneic hematopoietic stem cell transplantation, targeted and immunotherapy were used as preparation for transplantation. Allogeneic hematopoietic stem cell transplantation with graft-versus-host disease prophylaxis based on post-transplant cyclophosphamide, performed in complete remission, yielded a progression-free survival probability of 73.3%. Comparative analysis of autologous versus allogeneic hematopoietic stem cell transplantation in second and subsequent lines of therapy showed a trend favoring allogeneic transplantation but without achieving statistical significance ( $p = 0.11$ ).

**Conclusion**

This case illustrates the rare coexistence of multiple myeloma and T-cell lymphoblastic leukemia/lymphoma, underscoring the importance of timely diagnostics, diagnosis verification, and a comprehensive treatment approach.

Standard chemotherapy regimens demonstrate limited efficacy in the treatment of aggressive peripheral T-cell lymphomas. Performing autologous hematopoietic stem cell transplantation as consolidation in first-line therapy is considered the preferred clinical approach. The appropriateness of autologous transplantation at later stages remains a matter of debate and requires further investigation. Allogeneic hematopoietic stem cell transplantation is an effective method with curative potential for relapsed or refractory aggressive peripheral T-cell lymphomas. The use of targeted and immunotherapy improves the prognosis of patients with refractory or relapsed disease, particularly in preparation for allogeneic transplantation.