

Conference Abstracts

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Efficacy of Polatuzumab status post failed CAR-T in Richter's

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Abstract

Background

A 72-year-old man with del(17p) stage IV chronic lymphocytic leukemia (CLL), diagnosed in 1997, progressed through multiple therapies including R-CHOP, fludarabine, bendamustine-rituximab (BR), acalabrutinib, and venetoclax. In September 2022, he developed B symptoms and elevated lactate dehydrogenase (LDH). Axillary lymph node biopsy in January 2023 confirmed Richter transformation to diffuse large B-cell lymphoma (DLBCL) (CD5+, CD10-). He received two cycles of R-GDP, which were discontinued because of poor tolerance, followed by two cycles of polatuzumab vedotin plus BR (Pola-BR) as bridging therapy to chimeric antigen receptor T-cell (CAR-T) therapy. In May 2023, he underwent axicabtagene ciloleucel CAR-T, achieving a partial response, although LDH never normalized. He relapsed in February 2024 with recurrent B symptoms and PET-avid lymphadenopathy. Rechallenge with Pola-BR resulted in a complete metabolic response. He subsequently received maintenance rituximab and lenalidomide while being evaluated for allogeneic hematopoietic stem cell transplantation and CAR-T consolidation. After eight months of remission, disease progression occurred, and brentuximab vedotin was added to his maintenance regimen.

Methods

This case highlights the challenges of treating Richter's transformation in the background of relapse/refractory CLL, poor durability, and limited response to standard regimens for diffuse large B-cell lymphoma (DLBCL). Richter transformation occurs in 2–10% of chronic lymphocytic leukemia (CLL) patients, most commonly evolving into DLBCL.^{1,2} Per NCCN guidelines, it is managed similarly to high-risk large B-cell lymphoma using anthracycline- or platinum-based chemotherapy regimens like EPOCH, HYPER-CVAD, and OFAR, followed by consideration of stem cell transplant in eligible patients. However, these regimens are typically studied in younger populations and are often not viable for patients over 60. Polatuzumab vedotin, an antibody-drug conjugate targeting CD79b, has shown improved progression-free and overall survival when combined with bendamustine and rituximab (Pola-BR) in relapsed/refractory DLBCL.⁵ Yet, it has not been well studied in Richter's transformation. In our case, Pola-BR led to a strong clinical response, underscoring the potential role of antibody-drug conjugates in this setting, especially after CAR-T failure. Brentuximab Vedotin, another antibody drug conjugate has demonstrated efficacy with acceptable safety for relapsed or refractory DLBCL. In the ECHELON-3 trial BV + Len + R demonstrated a statistically significant survival benefit compared with Len + R + placebo in

patients with R/R DLBCL.⁸ There are several ongoing Phase II trials that are currently evaluating the safety and efficacy of ADC's in Richter's transformation.⁹

Conclusion

This case of relapsed DLBCL transformed from CLL illustrates the need for multiple lines of therapy and further trials, especially with CAR-T, in this high-risk population.

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