EDITORIAL

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A bridge, not a destination: clarifying the role of polatuzumab vedotin plus bendamustine and rituximab in relapsed/refractory diffuse large B-cell lymphoma

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Relapsed/refractory diffuse large B-cell lymphoma (DLBCL) remains a major therapeutic challenge, despite remarkable advances in cellular and immune-based therapies. Chimeric antigen receptor (CAR) T-cell therapy and, more recently, CD20 × CD3 bispecific antibodies (Abs) have redefined therapeutic paradigms, offering meaningful and sometimes durable remission in heavily pretreated patients. However, a substantial proportion of patients are ineligible for these therapies or require effective disease control while awaiting definitive treatment. As therapeutic options continue to evolve, there is a growing need to determine the optimal clinical positioning of polatuzumab vedotin plus bendamustine and rituximab (Pola-BR).

Polatuzumab vedotin, a CD79b-directed antibody–drug conjugate, was approved based on a randomized phase II trial that demonstrated superior response rates and survival compared to bendamustine-rituximab alone in transplant-ineligible relapsed/refractory DLBCL [1]. Consequently, Pola-BR has received regulatory approval for patients with relapsed/refractory DLBCL after ≥ 2 prior lines of therapy and is now widely regarded as a standard-of-care option in this setting [2]. However, in this rapidly evolving treatment landscape, the clinical question has shifted from whether Pola-BR is active, to where, when, and for whom it provides the highest value.

In this issue of the *Korean Journal of Internal Medicine*, Kim et al. [3] report a real-world, single-center experience with Pola-BR in 52 patients with relapsed/refractory DLBCL, providing timely insights into its current clinical role. The cohort was clinically heterogeneous and included patients treated with Pola-BR as salvage therapy, bridging therapy with CAR T-cell infusion, and treatment after CAR T-cell failure. Several observations from this study are particularly informative for current practice.

A notable finding was observed in patients who received Pola-BR as a bridging strategy for CAR T therapy. In this subgroup, the overall response rate was relatively high, and, importantly, more than 90% of patients successfully proceeded to CAR T-cell infusion. This finding suggests an important practical aspect of Pola-BR, namely, its ability to achieve rapid cytoreduction and disease stabilization during the vulnerable interval between leukapheresis and CAR T-cell infusion. Given the accumulating evidence that disease burden and clinical status at the time of infusion influence CAR T outcomes [4], an effective and tolerable bridging regimen remains an unmet need. These data suggest that Pola-BR is appropriate for this role in routine clinical practice.

A second notable finding was that the outcomes in patients treated with Pola-BR as a later-line salvage therapy or after CAR T-cell failure were considerably less favorable. Although objective responses were observed, progression-free survival was short and long-term disease control was uncommon. These findings are consistent with prior real-world reports and support the view that Pola-BR, when used in heavily pretreated or biologically aggressive diseas-

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es, should not be viewed as a definitive salvage therapy, but rather as a means of transient disease control [5]. From this perspective, it is noteworthy that recent studies evaluating polatuzumab vedotin in combination with CD20 × CD3 bispecific Abs, such as mosunetuzumab [6] and glofitamab [7], have reported high response rates and an encouraging duration of response in selected patients. These promising results have led to increasing interest in bispecific Abs as potential partners for polatuzumab vedotin. Further studies exploring optimal combinations in this particularly high-risk population are warranted.

Third, toxicity patterns observed in this study also merit attention. Hematological adverse events, particularly grade 3–4 cytopenia, were common, especially in heavily pretreated and post-CAR T-cell groups. In contrast, patients treated in the bridging setting experienced more manageable toxicity profiles, likely reflecting fewer treatment cycles and better baseline marrow reserves. These findings emphasize that Pola-BR toxicity is driven not only by the regimen itself, but also by cumulative prior therapy and exposure duration. From a practical standpoint, a short-course of Pola-BR with close monitoring may represent a reasonable compromise between efficacy and safety in selected patients.

Taken together, the data reported by Kim et al. [3] suggest a change in how Pola-BR should be viewed in current clinical practice. Rather than viewing Pola-BR as a curative salvage regimen, it may be best understood as a bridging treatment that helps patients proceed to more definitive therapies, such as CAR T-cells or next-generation immunotherapies.

However, there are still several challenges and opportunities. Strategies to mitigate bendamustine-related myelotoxicity, including dose optimization and bendamustine-sparing approaches, require prospective evaluation. Comparative studies of different bridging regimens are also needed to define the optimal approach for patients awaiting CAR T-cell therapy. Finally, improved patient stratification based on disease biology, tumor burden, and clinical fitness may help identify those most likely to benefit from Pola-BR, while avoiding unnecessary toxicities, as observed in a recent real-world study demonstrating meaningful outcomes with polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisolone as first-line therapies in very old patients with DLBCL [8].

In conclusion, Pola-BR plays a significant role in the management of relapsed/refractory DLBCL. In the era of cellular and immune therapies, its value appears to be greatest not as a stand-alone salvage regimen, but as a bridge that helps patients move on to more transformative treatments. The thorough integration of Pola-BR into individualized treatment pathways is essential to maximize its clinical impact in real-world practice.

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